## **EAST Search History**

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	171	cysk or cysteine synthase\$1	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 13:07
(12)	127	1 same (gene\$1 or sequence\$1 or nucleic or polynucleotide\$)	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:03
L3	118438	(serine or ser) same (coexpress\$ or rich or high or level\$1 or yield\$1 or optimiz\$)	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:05
L4	63	1 and 3	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:06
(15)	18	4 not 2	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:15
L6	6745	(amino acid\$1) near5 protein\$1 near5 (production\$ or express\$ or optimiz\$)	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:19
L7	949	6 same coli	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:18
L9	206	(amino acid\$1) near5 (composition\$ or profile\$) near5 protein\$1 near5 (production\$ or express\$ or optimiz\$)	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:24
(10)	5	9 same coli	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:21
(11)	12	(amino acid\$1) near5 (composition\$ or profile\$) near5 (heterologous or foreign) near3 protein\$1 near5 (production\$ or express\$ or optimiz\$)	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:27
Q.12	1	1 same coexpress\$	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:28
113	77	1 same (serine or ser)	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:29
114	20	13 not 2	US-PGPUB; USPAT	ADJ	OFF	2006/03/10 16:29

FILE 'HOME' ENTERED AT 17:09:38 ON 10 MAR 2006

=> fil .bec

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

0.21 SESSION 0.21

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 17:09:59 ON 10 MAR 2006 ALL COPYRIGHTS AND RESTRICTIONS APPLY. SEE HELP USAGETERMS FOR DETAILS.

11 FILES IN THE FILE LIST

=> s cysk or cysteine synthase#
FILE 'MEDLINE'

ILE .WEDFINE.

77 CYSK

64899 CYSTEINE

92418 SYNTHASE#

228 CYSTEINE SYNTHASE#

(CYSTEINE (W) SYNTHASE#)

L1 265 CYSK OR CYSTEINE SYNTHASE#

FILE 'SCISEARCH'

52 CYSK

47434 CYSTEINE

107943 SYNTHASE#

200 CYSTEINE SYNTHASE#

(CYSTEINE (W) SYNTHASE#)

L2 233 CYSK OR CYSTEINE SYNTHASE#

FILE 'LIFESCI'

48 CYSK

18083 "CYSTEINE"

23974 SYNTHASE#

88 CYSTEINE SYNTHASE#

("CYSTEINE"(W)SYNTHASE#)

L3 120 CYSK OR CYSTEINE SYNTHASE#

FILE 'BIOTECHDS'

51 CYSK

4197 CYSTEINE

6065 SYNTHASE#

59 CYSTEINE SYNTHASE#

(CYSTEINE (W) SYNTHASE#)

L4 79 CYSK OR CYSTEINE SYNTHASE#

FILE 'BIOSIS'

76 CYSK

59077 CYSTEINE

99656 SYNTHASE#

217 CYSTEINE SYNTHASE#

(CYSTEINE (W) SYNTHASE#)

L5 273 CYSK OR CYSTEINE SYNTHASE#

FILE 'EMBASE'

58 CYSK

49436 "CYSTEINE"

90470 SYNTHASE#

194 CYSTEINE SYNTHASE#

("CYSTEINE"(W)SYNTHASE#)

L6 223 CYSK OR CYSTEINE SYNTHASE#

FILE 'HCAPLUS'

```
100024 CYSTEINE
         94834 SYNTHASE#
           359 CYSTEINE SYNTHASE#
                  (CYSTEINE (W) SYNTHASE#)
L7
           451 CYSK OR CYSTEINE SYNTHASE#
FILE 'NTIS'
             0 CYSK
           490 CYSTEINE
           232 SYNTHASE#
             O CYSTEINE SYNTHASE#
                 (CYSTEINE (W) SYNTHASE#)
L8
             O CYSK OR CYSTEINE SYNTHASE#
FILE 'ESBIOBASE'
            41 CYSK
         23741 CYSTEINE
         44267 SYNTHASE#
            96 CYSTEINE SYNTHASE#
                  (CYSTEINE (W) SYNTHASE#)
L9
           122 CYSK OR CYSTEINE SYNTHASE#
FILE 'BIOTECHNO'
            43 CYSK
         22339 CYSTEINE
         29457 SYNTHASE#
           130 CYSTEINE SYNTHASE#
                  (CYSTEINE (W) SYNTHASE#)
L10
           151 CYSK OR CYSTEINE SYNTHASE#
FILE 'WPIDS'
            44 CYSK
          8434 CYSTEINE
          4985 SYNTHASE#
            43 CYSTEINE SYNTHASE#
                 (CYSTEINE (W) SYNTHASE#)
L11
            58 CYSK OR CYSTEINE SYNTHASE#
TOTAL FOR ALL FILES
          1975 CYSK OR CYSTEINE SYNTHASE#
L12
=> s (serine or ser) (15a) (rich or high or level# or yield# or optimiz?)
FILE 'MEDLINE'
         89374 SERINE
         21253 SER
         82402 RICH
       1384133 HIGH
       1482581 LEVEL#
        120679 YIELD#
         62852 OPTIMIZ?
          5214 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
L13
               ?)
FILE 'SCISEARCH'
         51760 SERINE
         21683 SER
        151346 RICH
       2077769 HIGH
       1544858 LEVEL#
        395337 YIELD#
        231907 OPTIMIZ?
          4738 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
L14
               ?)
```

175 CYSK

```
FILE 'LIFESCI'
         21346 SERINE
         10414 SER
         34806 RICH
        371067 HIGH
        429126 LEVEL#
         54802 YIELD#
         16670 OPTIMIZ?
          2904 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
L15
FILE 'BIOTECHDS'
          4795 SERINE
          4602 SER
          4493 RICH
         74156 HIGH
         51021 LEVEL#
         39614 YIELD#
         18716 OPTIMIZ?
L16
           601 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
FILE 'BIOSIS'
         68149 SERINE
         22012 SER
        105895 RICH
       1493999 HIGH
       1613796 LEVEL#
        298893 YIELD#
         67102 OPTIMIZ?
L17
          5953 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
FILE 'EMBASE'
         56820 SERINE
         18916 SER
         74243 RICH
       1329455 HIGH
       1698265 LEVEL#
        134210 YIELD#
         62502 OPTIMIZ?
          4606 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
L18
               ?)
FILE 'HCAPLUS'
        105605 SERINE
         34615 SER
        275173 RICH
       3744857 HIGH
       2249255 LEVEL#
       1150857 YIELD#
        289102 OPTIMIZ?
          9041 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
L19
               ?)
FILE 'NTIS'
           523 SERINE
           403 SER
          9236 RICH
        328134 HIGH
        228017 LEVEL#
         55396 YIELD#
         59744 OPTIMIZ?
L20
            76 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
               ?)
```

```
26942 SERINE
         12423 SER
         45135 RICH
        510678 HIGH
        573275 LEVEL#
         74897 YIELD#
         30661 OPTIMIZ?
L21
          3577 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
FILE 'BIOTECHNO'
         28989 SERINE
         11924 SER
         29372 RICH
        299126 HIGH
        367944 LEVEL#
         41645 YIELD#
         16086 OPTIMIZ?
          3241 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
L22
FILE 'WPIDS'
          8297 SERINE
          9747 SER
         33876 RICH
       2046959 HIGH
        610630 LEVEL#
        249912 YIELD#
         41189 OPTIMIZ?
L23
           492 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
               ?)
TOTAL FOR ALL FILES
L24
        40443 (SERINE OR SER) (15A) (RICH OR HIGH OR LEVEL# OR YIELD# OR OPTIMIZ
               ?)
=> s l12 and l24
FILE 'MEDLINE'
L25
           12 L1 AND L13
FILE 'SCISEARCH'
L26
            9 L2 AND L14
FILE 'LIFESCI'
L27
            5 L3 AND L15
FILE 'BIOTECHDS'
L28
             2 L4 AND L16
FILE 'BIOSIS'
L29
            9 L5 AND L17
FILE 'EMBASE'
             5 L6 AND L18
L30
FILE 'HCAPLUS'
           11 L7 AND L19
L31
FILE 'NTIS'
L32
            0 L8 AND L20
FILE 'ESBIOBASE'
           4 L9 AND L21
L33
```

FILE 'ESBIOBASE'

```
FILE 'BIOTECHNO'
             8 L10 AND L22
FILE 'WPIDS'
L35
             1 L11 AND L23
TOTAL FOR ALL FILES
           66 L12 AND L24
=> s 112 and coexpress?
FILE 'MEDLINE'
         13548 COEXPRESS?
L37
             2 L1 AND COEXPRESS?
FILE 'SCISEARCH'
         13934 COEXPRESS?
L38
             2 L2 AND COEXPRESS?
FILE 'LIFESCI'
          6199 COEXPRESS?
             2 L3 AND COEXPRESS?
L39
FILE 'BIOTECHDS'
           660 COEXPRESS?
L40
             1 L4 AND COEXPRESS?
FILE 'BIOSIS'
         13729 COEXPRESS?
L41
             2 L5 AND COEXPRESS?
FILE 'EMBASE'
         12791 COEXPRESS?
             1 L6 AND COEXPRESS?
L42
FILE 'HCAPLUS'
         12757 COEXPRESS?
             2 L7 AND COEXPRESS?
L43
FILE 'NTIS'
            33 COEXPRESS?
L44
             0 L8 AND COEXPRESS?
FILE 'ESBIOBASE'
          9809 COEXPRESS?
             1 L9 AND COEXPRESS?
L45
FILE 'BIOTECHNO'
          7587 COEXPRESS?
L46
             1 L10 AND COEXPRESS?
FILE 'WPIDS'
           140 COEXPRESS?
L47
             0 L11 AND COEXPRESS?
TOTAL FOR ALL FILES
           14 L12 AND COEXPRESS?
L48
=> s (amino acid or ser or serine) (15a) (composition# or profil?)
FILE 'MEDLINE'
        612125 AMINO
       1387745 ACID
```

459057 AMINO ACID

21253 SER

(AMINO(W)ACID)

```
89374 SERINE
        162979 COMPOSITION#
        236020 PROFIL?
         13569 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
L49
FILE 'SCISEARCH'
        385550 AMINO
       1114189 ACID
        204369 AMINO ACID
                  (AMINO(W) ACID)
         21683 SER
         51760 SERINE
        404372 COMPOSITION#
        365251 PROFIL?
L50
          9303 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
FILE 'LIFESCI'
        166826 "AMINO"
        297172 "ACID"
        115086 AMINO ACID
                  ("AMINO"(W) "ACID")
         10414 SER
         21346 SERINE
         97038 COMPOSITION#
         52629 PROFIL?
L51
          6007 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
FILE 'BIOTECHDS'
         66035 AMINO
        135710 ACID
         47319 AMINO ACID
                  (AMINO(W) ACID)
          4602 SER
          4795 SERINE
         40424 COMPOSITION#
         10048 PROFIL?
          2448 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
L52
FILE 'BIOSIS'
        521001 AMINO
       1241250 ACID
        303253 AMINO ACID
                  (AMINO(W)ACID)
         22012 SER
         68149 SERINE
        321074 COMPOSITION#
        229122 PROFIL?
L53
         21821 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
FILE 'EMBASE'
        421666 "AMINO"
       1369373 "ACID"
        285316 AMINO ACID
                  ("AMINO"(W) "ACID")
         18916 SER
         56820 SERINE
        146585 COMPOSITION#
        199373 PROFIL?
         13021 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
L54
FILE 'HCAPLUS'
       1060945 AMINO
       4112384 ACID
        526592 AMINO ACID
                  (AMINO(W)ACID)
```

```
34615 SER
        105605 SERINE
        940605 COMPOSITION#
       1384879 COMPN
       1938054 COMPOSITION#
                  (COMPOSITION# OR COMPN)
        422290 PROFIL?
         37840 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
L55
FILE 'NTIS'
          6961 AMINO
         43883 ACID
          2458 AMINO ACID
                  (AMINO(W)ACID)
           403 SER
           523 SERINE
         69557 COMPOSITION#
         57548 PROFIL?
           223 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
L56
FILE 'ESBIOBASE'
        177493 AMINO
        336489 ACID
         98921 AMINO ACID
                  (AMINO(W)ACID)
         12423 SER
         26942 SERINE
         82506 COMPOSITION#
         91500 PROFIL?
L57
          3439 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
FILE 'BIOTECHNO'
        204625 AMINO
        349810 ACID
        154660 AMINO ACID
                 (AMINO(W)ACID)
         11924 SER
         28989 SERINE
         38895 COMPOSITION#
         42958 PROFIL?
L58
          6366 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
FILE 'WPIDS'
        244392 AMINO
        937777 ACID
         68710 AMINO ACID
                  (AMINO(W)ACID)
          9747 SER
          8297 SERINE
        707136 COMPOSITION#
          8956 COMPN
        388438 COMPSN
        111886 COMPSNS
        879081 COMPOSITION#
                  (COMPOSITION# OR COMPN OR COMPSNS)
        194379 PROFIL?
          4757 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
L59
TOTAL FOR ALL FILES
        118794 (AMINO ACID OR SER OR SERINE) (15A) (COMPOSITION# OR PROFIL?)
=> s 112 and 160
FILE 'MEDLINE'
             7 L1 AND L49
L61
```

```
8 L2 AND L50
FILE 'LIFESCI'
             3 L3 AND L51
FILE 'BIOTECHDS'
             1 L4 AND L52
FILE 'BIOSIS'
            18 L5 AND L53
L65
FILE 'EMBASE'
L66
             6 L6 AND L54
FILE 'HCAPLUS'
            16 L7 AND L55
L67
FILE 'NTIS'
L68
             0 L8 AND L56
FILE 'ESBIOBASE'
             3 L9 AND L57
L69
FILE 'BIOTECHNO'
L70
             4 L10 AND L58
FILE 'WPIDS'
             0 L11 AND L59
L71
TOTAL FOR ALL FILES
L72
           66 L12 AND L60
=> s (heterologous or foreign or recombinant)(5a)(protein#)(10a)(produc? or
express? or optimiz?)
FILE 'MEDLINE'
         47718 HETEROLOGOUS
         59253 FOREIGN
        260330 RECOMBINANT
       1917452 PROTEIN#
       1292191 PRODUC?
        987095 EXPRESS?
         62852 OPTIMIZ?
L73
          9273 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'SCISEARCH'
         22183 HETEROLOGOUS
         30720 FOREIGN
        151971 RECOMBINANT
       1506451 PROTEIN#
       1820406 PRODUC?
       1264806 EXPRESS?
        231907 OPTIMIZ?
          9497 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L74
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'LIFESCI'
         14826 HETEROLOGOUS
          8447 FOREIGN
         66783 RECOMBINANT
        557087 PROTEIN#
        514871 PRODUC?
        391866 EXPRESS?
```

FILE 'SCISEARCH'

```
16670 OPTIMIZ?
          7060 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L75
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'BIOTECHDS'
         10884 HETEROLOGOUS
          6430 FOREIGN
         97090 RECOMBINANT
        151602 PROTEIN#
        222303 PRODUC?
        140581 EXPRESS?
         18716 OPTIMIZ?
         28528 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L76
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'BIOSIS'
         29246 HETEROLOGOUS
         27340 FOREIGN
        190479 RECOMBINANT
       1776662 PROTEIN#
       1712468 PRODUC?
       1177112 EXPRESS?
         67102 OPTIMIZ?
         11496 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L77
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'EMBASE'
         22283 HETEROLOGOUS
         32257 FOREIGN
        168217 RECOMBINANT
       1528079 PROTEIN#
       1234355 PRODUC?
        900431 EXPRESS?
         62502 OPTIMIZ?
          7669 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L78
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'HCAPLUS'
         31811 HETEROLOGOUS
         44935 FOREIGN
        181959 RECOMBINANT
       2145009 PROTEIN#
       4210196 PRODUC?
       925167 PRODN
       4658156 PRODUC?
                 (PRODUC? OR PRODN)
       1198161 EXPRESS?
        289102 OPTIMIZ?
L79
         21347 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'NTIS'
           303 HETEROLOGOUS
        384442 FOREIGN
          1594 RECOMBINANT
         18611 PROTEIN#
        370125 PRODUC?
         39074 EXPRESS?
         59744 OPTIMIZ?
           139 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L80
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'ESBIOBASE'
         12834 HETEROLOGOUS
```

10210 FOREIGN

```
719877 PROTEIN#
        581093 PRODUC?
        561398 EXPRESS?
         30661 OPTIMIZ?
          7785 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L81
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'BIOTECHNO'
         14199 HETEROLOGOUS
          6070 FOREIGN
        125134 RECOMBINANT
        653195 PROTEIN#
        394590 PRODUC?
        452182 EXPRESS?
         16086 OPTIMIZ?
          8130 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L82
               UC? OR EXPRESS? OR OPTIMIZ?)
FILE 'WPIDS'
          9977 HETEROLOGOUS
         40929 FOREIGN
         40069 RECOMBINANT
        154449 PROTEIN#
       2335750 PRODUC?
        124549 EXPRESS?
         41189 OPTIMIZ?
          4754 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L83
               UC? OR EXPRESS? OR OPTIMIZ?)
TOTAL FOR ALL FILES
      115678 (HETEROLOGOUS OR FOREIGN OR RECOMBINANT) (5A) (PROTEIN#) (10A) (PROD
L84
               UC? OR EXPRESS? OR OPTIMIZ?)
=> s 112 and 184
FILE 'MEDLINE'
L85
             4 L1 AND L73
FILE 'SCISEARCH'
             3 L2 AND L74
L86
FILE 'LIFESCI'
            5 L3 AND L75
L87
FILE 'BIOTECHDS'
             5 L4 AND L76
1.88
FILE 'BIOSIS'
             2 L5 AND L77
L89
FILE 'EMBASE'
             2 L6 AND L78
L90
FILE 'HCAPLUS'
            5 L7 AND L79
L91
FILE 'NTIS'
             0 L8 AND L80
L92
FILE 'ESBIOBASE'
            3 L9 AND L81
L93
FILE 'BIOTECHNO'
```

83652 RECOMBINANT

L94

2 L10 AND L82

FILE 'WPIDS'

L95 2 L11 AND L83

TOTAL FOR ALL FILES

L96 33 L12 AND L84

=> s 160 and 184

FILE 'MEDLINE'

L97 50 L49 AND L73

FILE 'SCISEARCH'

L98 47 L50 AND L74

FILE 'LIFESCI'

L99 38 L51 AND L75

FILE 'BIOTECHDS'

L100 485 L52 AND L76

FILE 'BIOSIS'

L101 55 L53 AND L77

FILE 'EMBASE'

L102 64 L54 AND L78

FILE 'HCAPLUS'

L103 165 L55 AND L79

FILE 'NTIS'

L104 0 L56 AND L80

FILE 'ESBIOBASE'

L105 42 L57 AND L81

FILE 'BIOTECHNO'

L106 74 L58 AND L82

FILE 'WPIDS'

L107 43 L59 AND L83

TOTAL FOR ALL FILES

L108 1063 L60 AND L84

=> s 1108 and coli

FILE 'MEDLINE'

249337 COLI

L109 30 L97 AND COLI

FILE 'SCISEARCH'

228507 COLI

L110 25 L98 AND COLI

FILE 'LIFESCI'

98566 COLI

L111 21 L99 AND COLI

FILE 'BIOTECHDS'

45738 COLI

L112 129 L100 AND COLI

FILE 'BIOSIS'

276667 COLI

L113 29 L101 AND COLI

FILE 'EMBASE'

177298 COLI

L114 34 L102 AND COLI

FILE 'HCAPLUS'

266594 COLI

L115 69 L103 AND COLI

FILE 'NTIS'

2810 COLI

L116 0 L104 AND COLI

FILE 'ESBIOBASE'

68890 COLI

L117 19 L105 AND COLI

FILE 'BIOTECHNO'

94549 COLI

L118 32 L106 AND COLI

FILE 'WPIDS'

18914 COLI

L119 8 L107 AND COLI

TOTAL FOR ALL FILES

L120 396 L108 AND COLI

=> s (136 or 148 or 172 or 196 or 1120)

FILE 'MEDLINE'

L121 51 (L25 OR L37 OR L61 OR L85 OR L109)

FILE 'SCISEARCH'

L122 43 (L26 OR L38 OR L62 OR L86 OR L110)

FILE 'LIFESCI'

L123 32 (L27 OR L39 OR L63 OR L87 OR L111)

FILE 'BIOTECHDS'

L124 133 (L28 OR L40 OR L64 OR L88 OR L112)

FILE 'BIOSIS'

L125 56 (L29 OR L41 OR L65 OR L89 OR L113)

FILE 'EMBASE'

L126 44 (L30 OR L42 OR L66 OR L90 OR L114)

FILE 'HCAPLUS'

L127 98 (L31 OR L43 OR L67 OR L91 OR L115)

FILE 'NTIS'

L128 0 (L32 OR L44 OR L68 OR L92 OR L116)

FILE 'ESBIOBASE'

L129 26 (L33 OR L45 OR L69 OR L93 OR L117)

FILE 'BIOTECHNO'

L130 43 (L34 OR L46 OR L70 OR L94 OR L118)

FILE 'WPIDS'

L131 10 (L35 OR L47 OR L71 OR L95 OR L119)

TOTAL FOR ALL FILES

L132 536 (L36 OR L48 OR L72 OR L96 OR L120)

=> s 1132 not 2004-2006/py

FILE 'MEDLINE'

```
1332548 2004-2006/PY
```

(20040000-20069999/PY)

L133 44 L121 NOT 2004-2006/PY

FILE 'SCISEARCH'

2454856 2004-2006/PY

(20040000-20069999/PY)

L134 35 L122 NOT 2004-2006/PY

FILE 'LIFESCI'

189530 2004-2006/PY

L135 26 L123 NOT 2004-2006/PY

FILE 'BIOTECHDS'

56959 2004-2006/PY

L136 79 L124 NOT 2004-2006/PY

FILE 'BIOSIS'

1023506 2004-2006/PY

L137 50 L125 NOT 2004-2006/PY

FILE 'EMBASE'

1117159 2004-2006/PY

L138 33 L126 NOT 2004-2006/PY

FILE 'HCAPLUS'

2548350 2004-2006/PY

L139 74 L127 NOT 2004-2006/PY

FILE 'NTIS'

25986 2004-2006/PY

L140 0 L128 NOT 2004-2006/PY

FILE 'ESBIOBASE'

664275 2004-2006/PY

L141 18 L129 NOT 2004-2006/PY

FILE 'BIOTECHNO'

586 2004-2006/PY

L142 43 L130 NOT 2004-2006/PY

FILE 'WPIDS'

2489972 2004-2006/PY

L143 1 L131 NOT 2004-2006/PY

TOTAL FOR ALL FILES

L144 403 L132 NOT 2004-2006/PY

=> dup rem 1144

PROCESSING COMPLETED FOR L144

L145 199 DUP REM L144 (204 DUPLICATES REMOVED)

=> d tot

L145 ANSWER 1 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

New PRO20080 polypeptides and polynucleotides, useful for treating immune-related disorders in a mammal, e.g. systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, bullous skin disease, or allergies;

recombinant protein production and

antagonist and agonist for use in disease gene therapy

AU GREWAL I; GURNEY A L; VALDEZ P A

AN 2003-20959 BIOTECHDS

PI WO 2003055440 10 Jul 2003

L145 ANSWER 2 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel recombinant crystallized polypeptides from Streptococcus pneumoniae ΤI useful as drug target for pathogenic bacteria, has biological activity of NH(3)-dependent NAD(+) synthetase; plasmid-mediated gene transfer and expression in Escherichia coli for recombinant protein production for recombinant vaccine and disease EDWARDS A; DHARAMSI A; VEDADI M; ALAM M Z; HOUSTON S; PINDER B; NG I; LAM ΑU R; KIMBER M 2003-20545 BIOTECHDS AN WO 2003051916 26 Jun 2003 PΙ L145 ANSWER 3 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New peptides useful, e.g. in the treatment of or reduction of viral load TI of hepatitis C virus and associated conditions, e.g. liver fibrosis, necrosis, inflammation or bile duct changes; vector-mediated gene transfer and expression in host cell for recombinant protein production, drug screening and disease therapy JOYCE M; WILLIAMS M; HINDSGAUL O; TYRREL D L AU 2003-22522 BIOTECHDS AN WO 2003051910 26 Jun 2003 PΙ L145 ANSWER 4 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New GAVE18 polypeptide and nucleic acid molecule encoding the ΤI polypeptide, useful for preventing and treating a disease or disorder associated with aberrant expression or activity of GAVE18, e.g. asthma or rheumatoid arthritis; recombinant protein production and agonist and antagonist for use in disease gene therapy EISHINGDRELO H; CAI J; BUSCH S J; GASSENHUBER J ΑU AN 2003-17738 BIOTECHDS PΙ WO 2003042399 22 May 2003 L145 ANSWER 5 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN TΤ New cupiennin peptides exhibiting an antimicrobial, hemolytic or insecticidal activity, useful for preparing a composition for treating bacterial infections and tumors; vector-mediated gene transfer and expression in host cell for recombinant protein and insecticide production for use in bacterium infection and leukemia gene therapy ΔII SCHALLER J; WALZ A; NENTWIG W; KUHN-NENTWIG L ΔN 2003-16957 BIOTECHDS рT WO 2003035677 1 May 2003 ANSWER 6 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 New polynucleotide designated 205P1B5, for diagnosing and treating ΤI prostate cancer, and as probes or primers for the amplification and/or detection of 205P1B5 genes; recombinant protein production and its encoding gene useful for gene therapy, diagnosis and prognosis ΑU CHALLITA-EID P M; RAITANO A B; FARIS M; HUBERT R S; JAKOBOVITS A 2003-14871 BIOTECHDS AN WO 2003020954 13 Mar 2003 PT L145 ANSWER 7 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN TI New isolated polypeptide based on the neutralizing epitope of the p17 protein of HIV, useful for the diagnosis, prevention and treatment of the human acquired immune deficiency syndrome; plasmid-mediated gene transfer and expression in Escherichia coli for recombinant gluthathione-transferase fusion protein production for use in HIV virus infection therapy

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CARUSO A; FRANZONE J S
ΑU
      2003-11714 BIOTECHDS
AN
PΙ
      WO 2003016337 27 Feb 2003
     ANSWER 8 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L145
ΤI
      New UvrA and UvrB polypeptides and polynucleotides encoding the
      polypeptides, useful for detecting DNA damage for diagnosing cancer,
      increasing the effectiveness of drug treatment or detecting the effect of
      environmental genotoxin;
           recombinant protein production in
         Escherichia coli useful for cancer diagnosis
ΑU
      VAN HOUTEN B; SKORVAGA M
AN
      2003-11705 BIOTECHDS
PΙ
      WO 2003014324 20 Feb 2003
L145 ANSWER 9 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
      Novel nitrilase polypeptide, useful for making (R) - or
TT
      (S)-ethyl-4-cyano-3-hydroxybutyric acid or (R)- or (S)-mandelic acid or
      (S) - or (R) -phenyl lactic acid derivative and for producing
      pharmaceutical composition, and food additive;
         vector-mediated recombinant protein gene transfer
         and expression in host cell for use in pharmaceutical and
         food industry and peptidomics
      MADDEN M; DESANTIS G; CHAPLIN J A; WEINER D P; MILAN A; CHI E; SHORT J M;
ΑU
      BURK M
      2003-10320 BIOTECHDS
ΔN
      WO 2003000840 3 Jan 2003
PΙ
L145 ANSWER 10 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
      New polynucleotide, useful for manipulating plant protein quality,
TT
      improving plant growth, yield and crop productivity or grain composition
      or producing plants with improved properties;
           recombinant protein production via
         plasmid expression in host cell for use in transgenic plant
         construction
      EDGERTON M D; CHOMET P S; LACCETTI L B
AU
      2004-07435 BIOTECHDS
AN
      US 2003233670 18 Dec 2003
PΙ
     ANSWER 11 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L145
      New nucleic acids encoding PRO polypeptides having sequence identity to
ΤI
      Interleukin-17, useful for diagnosing or treating of immune related
      diseases e.g. rheumatoid arthritis, thyroiditis, diabetes mellitus or
      allergic rhinitis;
           recombinant protein production and
         antagonist and agonist for use in disease therapy and gene therapy
      CHEN J; FILVAROFF E; FONG S; GODDARD A; GODOWSKI P; GRIMALDI J C; GURNEY
AU
      A; LI H; HILLAN K; HYMOWITZ S G; TUMAS D; STAROVASNIK M A; VANLOOKEREN M;
      VANDLEN R; WATANABE C; WILLIAMS P M; WOOD W I; YANSURA D
      2004-05717 BIOTECHDS
AN
      US 2003203451 30 Oct 2003
PΙ
      ANSWER 12 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L145
      New genes from Staphylococcus aureus encode virulence factors designated
ΤI
      repressor of toxin, Rot, and Rot-like protein Rlp and are useful to
      detect S. aureus in a sample;
           recombinant protein production via
         plasmid expression in host cell for in bacterium detection
      MCNAMARA P J
ΑU
ΑN
      2004-00325 BIOTECHDS
PΤ
      US 2003171563 11 Sep 2003
     ANSWER 13 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L145
      New estrogen receptor beta variant polypeptide and nucleic acid fragment,
TI
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useful in therapeutic modulation of pathophysiologic estrogen signaling

(e.q. gene delivery or gene silencing), or developing pharmaceutical drug targets; vector-mediated gene transfer and expression in host cell for recombinant protein production and disease therapy or gene therapy QUINET E M; FAN E 2004-03630 BIOTECHDS US 2003162257 28 Aug 2003 ANSWER 14 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel vascular endothelial cell growth factor-E polypeptide, useful for treating cardiovascular or endothelial disorders; recombinant protein production via plasmid expression in host cell for use in disease therapy FERRARA N; KUO S S 2004-01862 BIOTECHDS US 2003113870 19 Jun 2003 L145 ANSWER 15 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Composition comprising orthogonal aminoacyl-tRNA synthetase that preferentially aminoacylates orthogonal tRNA with non-natural amino acids, useful for incorporating non-natural amino acids into polypeptides in vivo; recombinant enzyme protein and vector expression in host cell for use in non-natural amino acid incorporation and site-selective insertion SCHULTZ P; WANG L; ANDERSON J C; CHIN J W; LIU D R; MAGLIERY T J; MEGGERS E L; MEHL R A; PASTRNAK M; SANTORO S W; ZHANG Z 2004-02882 BIOTECHDS US 2003108885 12 Jun 2003 ANSWER 16 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN 1.145 New purified nucleic acid segment encoding hyaluronic acid synthase, useful for hyaluronic acid, and for detecting a bacterial cell that is expressing hyaluronic synthase; recombinant enzyme protein production via plasmid expression in host cell useful for bacterium cell detection WEIGEL P H; DEANGELIS P L; PAPACONSTANTINOU J 2003-28187 BIOTECHDS US 2003104533 5 Jun 2003 L145 ANSWER 17 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel purified nucleic acid segment encoding hyaluronic acid synthase, useful for hyaluronic acid, and for detecting a bacterial cell that is expressing hyaluronic synthase; vector-mediated hyaluronic-acid-synthase gene transfer and expression in host cell for recombinant protein production and cloning WEIGEL P H; DEANGELIS P L; PAPACONSTANTINOU J 2003-27658 BIOTECHDS US 2003104415 5 Jun 2003 ANSWER 18 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel isolated DNA98853 or DNA101848 polypeptide having homology to members of tumor necrosis factor receptor family useful in assays to identify proteins or molecules involved in binding interactions; vector-mediated gene transfer and expression in host cell for recombinant protein production and disease therapy GODDARD A; PAN J; YAN M 2003-28389 BIOTECHDS US 2003092044 15 May 2003

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L145 ANSWER 19 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

New PRO nucleic acid, useful for preparing a composition for treating an TI immune related disease in a mammal e.g., rheumatoid arthritis, diabetes mellitus or autoimmune disease; vector-mediated gene transfer and expression in CHO cell, yeast or Escherichia coli for recombinant protein production for use in disease gene therapy FONG S: GODDARD A: GODOWSKI P J: GRIMALDI J C: GURNEY A L: HILLAN K J; ΑU TUMAS D: WATANABE C K; WOOD W I; ZHANG Z AN 2003-22976 BIOTECHDS US 2003077737 24 Apr 2003 PΙ ANSWER 20 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel isolated PRO polypeptides PRO1265, PRO1308, PRO1475, PRO4405, ΤI PRO5723, PRO7425 or PRO9940, useful for treating an immune-related disease such as rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia; recombinant protein production and antagonist and agonist for use in disease therapy and gene therapy GODDARD A; GODOWSKI P J; GURNEY A L; HILLAN K J; TUMAS D; WATANABE C K; ΑU WOOD W I 2003-27366 BIOTECHDS AN US 2003059437 27 Mar 2003 PΙ ANSWER 21 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 TТ New isolated nucleic acid encoding a PRO polypeptide, e.g. PRO1031, PRO1122, PRO10272, useful in molecular biology, chromosome and gene mapping, in generating antisense RNA and DNA, and in gene therapy; involving vector-mediated recombinant protein gene transfer and expression in Chinese hamster ovary, Escherichia coli or yeast cell for use in diagnosis, prevention, therapy and gene therapy CHEN J; FILVAROFF E; FONG S; GODDARD A; GODOWSKI P J; GRIMALDI C; GURNEY AU A L; LI H; HILLAN K; TUMAS D; VANLOOKEREN M; VANDLEN R; WATANABE C; WILLIAMS P M; WOOD W I; YANSURA D G AN 2003-14221 BIOTECHDS PΙ US 2003008815 9 Jan 2003 L145 ANSWER 22 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Crystalline composition comprising hepatitis C virus (HCV) NS3/NS4A ΤI polypeptide complex, useful for determining three-dimensional structure of HCV NS3/NS4A complex, and modeling tertiary structure of related proteins; protein 3D structure coordinate and antagonist and agonist useful for drug screening ΑU REICHERT P; PROSISE W W; TAREMI S S; YAO N; WEBER P C 2003-22442 BIOTECHDS ΔŊ US 6524589 25 Feb 2003 PΙ L145 ANSWER 23 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel Tumor Necrosis Factor (TNF) delta nucleic acid useful for assaying ΤI genetic variation and aberrations such as defects or to remediate TNF delta dysfunction, and in gene therapy; human recombinant protein production and its encoding gene useful for gene therapy and diagnosis ΑU YU G; NI J; GENTZ R; DILLON P J 2003-14839 BIOTECHDS AN US 6509170 21 Jan 2003 PΙ ANSWER 24 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel protein having D-hydantoinase or D-carbamylase activity, for manufacturing N-carbamyl-D-amino acids and D-amino acids, in chemical

recombinant enzyme protein production via plasmid expression in host cell useful for food and pharmaceutical industry

industry and in food additives;

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AN
     2003-19878 BIOTECHDS
PΙ
     JP 2003024074 28 Jan 2003
L145 ANSWER 25 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
     Polypeptide ligand of GPR8 comprising N-terminal methionine residue fused
TΙ
     to a polypeptide having N-terminal cysteine residue, useful in the
     treatment of cancer and Alzheimer's disease;
          recombinant protein production via
        plasmid expression in host cell for use in disease therapy
        and drug screening
     2003-25647 BIOTECHDS
AN
     JP 2003009867 14 Jan 2003
PΙ
L145 ANSWER 26 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
     New PRO polypeptides useful for diagnosing tumor in mammal and for
TI
     producing antibodies useful in treatment of neoplastic cell growth;
          recombinant protein production and
        antibody for use in disease therapy and gene therapy
     CHEN J; BAKER K P; YUAN J; GURNEY A; GODDARD A; WOOD W I
AU
AN
     2004-23473 BIOTECHDS
     AU 2002330288 17 Apr 2003
PΙ
L145 ANSWER 27 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
    Immunogenic composition containing chimeric HIV polypeptide (p24-gp41 or
ΤI
    p24-gp36), and test-kits for detection of antibodies raised against HIV
SO
    Russ., No pp. given
    CODEN: RUXXE7
    Sidorovich, I. G.; Nikolaeva, I. A.; Sheval'e, A. F.; Ignat'eva, G. A.;
TN
    Korobova, S. V.; Alekseev, T. A.; Petrov, R. V.; Khaitov, R. M.
AN
    2003:862724 HCAPLUS
DN
    140:180118
                      KIND DATE APPLICATION NO.
    PATENT NO.
                                          -----
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                              20031020 RU 2001-122896
                                                               20010816
PΙ
    RU 2214274
                        C2
L145 ANSWER 28 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
    Human stem cell growth factor mutant protein, its preparation and medical
TI
    composition
    Faming Zhuanli Shenqing Gongkai Shuomingshu, 17 pp.
SO
    CODEN: CNXXEV
    Liu, Qingfa; Li, Jing; Hu, Huarong; Hu, Hui
TN
    2005:841769 HCAPLUS
AN
DN
    143:261406
                              DATE APPLICATION NO.
    PATENT NO.
                      KIND
                                                              DATE
     _____
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                                          -----
                               20031001 CN 2002-111092
                                                               20020320
PΙ
    CN 1445239
                        Α
L145 ANSWER 29 OF 199
                        MEDLINE on STN
                                                      DUPLICATE 1
    Engineering Escherichia coli for increased productivity of
    serine-rich proteins based on proteome profiling
    Applied and environmental microbiology, (2003 Oct) Vol. 69, No. 10, pp.
so
    5772-81.
    Journal code: 7605801. ISSN: 0099-2240.
    Han Mee-Jung; Jeong Ki Jun; Yoo Jong-Shin; Lee Sang Yup
IΙΔ
                   MEDLINE
AN
    2003497591
L145 ANSWER 30 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
    Quantification of the isomerization of Asp residue in recombinant human
TI
    αA-crystallin by reversed-phase HPLC
    Journal of Pharmaceutical and Biomedical Analysis (2003), 30(6), 1825-1833
SO
    CODEN: JPBADA; ISSN: 0731-7085
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Sadakane, Yutaka; Yamazaki, Toshiaki; Nakagomi, Kazuya; Akizawa,

Toshifumi; Fujii, Noriko; Tanimura, Takenori; Kaneda, Masaki; Hatanaka,

ΑU

Yasumaru

- AN 2002:951194 HCAPLUS
- DN 139:145381
- L145 ANSWER 31 OF 199 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 2
- TI Sulfur assimilation in soybean: Molecular cloning and characterization of O-acetylserine (thiol) lyase (cysteine synthase)
- SO CROP SCIENCE, (SEP-OCT 2003) Vol. 43, No. 5, pp. 1819-1827. ISSN: 0011-183X.
- AU Chronis D; Krishnan H B (Reprint)
- AN 2003:774749 SCISEARCH
- L145 ANSWER 32 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
- TI Cloning, expression, and renaturation studies of Reteplase
- SO Journal of Microbiology and Biotechnology (2003), 13(6), 989-992 CODEN: JOMBES; ISSN: 1017-7825
- AU Zhao, Youchun; Wang, Ge; Kong, Yang; Zhang, Changkai
- AN 2004:75941 HCAPLUS
- DN 140:247840
- L145 ANSWER 33 OF 199 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
- TI Molecular cloning, expression and characterization of three short chain  $\alpha$ -neurotoxins from the venom of sea snake Hydrophiinae Hydrophis cyanocinctus Daudin.
- SO Toxicon, (2003) Vol. 42, No. 7, pp. 753-761. . Refs: 31 ISSN: 0041-0101 CODEN: TOXIA6
- AU Peng L.-S.; Zhong X.-F.; Huang Y.-S.; Zhang Y.; Zheng S.-L.; Wei J.-W.; Wu W.-Y.; Xu A.-L.
- AN 2004045475 EMBASE
- L145 ANSWER 34 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
- TI Cloning and molecular and immunological characterisation of two new food allergens, Cap a 2 and Lyc e 1, profilins from bell pepper (Capsicum annuum) and tomato (Lycopersicon esculentum)
- SO International Archives of Allergy and Immunology (2003), 131(4), 245-255 CODEN: IAAIEG; ISSN: 1018-2438
- AU Willerroider, M.; Fuchs, H.; Ballmer-Weber, B. K.; Focke, M.; Susani, M.; Thalhamer, J.; Ferreira, F.; Wuethrich, B.; Scheiner, O.; Breiteneder, H.; Hoffmann-Sommergruber, K.
- AN 2003:623472 HCAPLUS
- DN 140:76195
- L145 ANSWER 35 OF 199 MEDLINE on STN
- TI A novel O-phospho-L-serine sulfhydrylation reaction catalyzed by O-acetylserine sulfhydrylase from Aeropyrum pernix K1.
- SO FEBS letters, (2003 Sep 11) Vol. 551, No. 1-3, pp. 133-8. Journal code: 0155157. ISSN: 0014-5793.
- AU Mino Koshiki; Ishikawa Kazuhiko
- AN 2003424973 MEDLINE
- L145 ANSWER 36 OF 199 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3
- TI Cel6A, a major exoglucanase from the cellulosome of the anaerobic fungi Piromyces sp. E2 and Piromyces equi.
- SO Biochimica et Biophysica Acta Gene Structure and Expression, (9 Jul 2003) Vol. 1628, No. 1, pp. 30-39. .
  Refs: 61
  - ISSN: 0167-4781 CODEN: BBGSD5
- AU Harhangi H.R.; Freelove A.C.J.; Ubhayasekera W.; Van Dinther M.; Steenbakkers P.J.M.; Akhmanova A.; Van Der Drift C.; Jetten M.S.M.; Mowbray S.L.; Gilbert H.J.; Op Den Camp H.J.M.
- AN 2003266875 EMBASE

ANSWER 37 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New isolated nucleic acid molecule encoding a NS4 polypeptide, useful for TI treating a body weight disorder, e.g. obesity, anorexia, cachexia, or conditions related to obesity, e.g. polycystic ovarian disease, dermatological disorders; vector-mediated recombinant protein gene transfer and expression in Chinese hamster ovary cell culture, Escherichia coli or yeast cell for use in gene therapy GODDARD A; PAN J; WOOD W I ΑU 2003-10100 BIOTECHDS AN WO 2002101069 19 Dec 2002 PΤ L145 ANSWER 38 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel immunogenic, mutant cholera holotoxin useful for enhancing immune TI response of vertebrate host to antigen, comprises amino sequence of subunit A of wild-type cholera toxin; vector-mediated gene transfer and expression in host cell for recombinant vaccine and immunostimulant GREEN B A; HOLMES R K; JOBLING M G; ZHU D ΔII AN 2003-09012 BIOTECHDS PТ WO 2002098369 12 Dec 2002 L145 ANSWER 39 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New TALL-1-binding polypeptide, useful for modulating the activity of TI TALL-1 and in treating, preventing or diagnosing a B-cell-mediated autoimmune diseases, cancers or lymphomas; vector-mediated recombinant protein gene transfer and expression in host cell for use in gene therapy MIN H; HSU H AU 2003-09315 BIOTECHDS AN WO 2002092620 21 Nov 2002 PΙ L145 ANSWER 40 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New compound containing acidic and aromatic amino acids, useful as TI antiviral therapy in pharmaceutical, veterinary or agricultural/horticultural applications; compound production and virus vector expression in host cell for use in gene therapy DASGUPTA A; DAS S; BAIDYA N ΑU 2003-07297 BIOTECHDS ΑN WO 2002083858 24 Oct 2002 PΙ ANSWER 41 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel fusion protein for inducing human immunodeficiency virus-antigen TI specific IgG and IgA antibodies, has ectodomain of HIV-1 envelope glycoprotein gp41 fused to fragment of influenza virus hemagglutinin protein; vector-mediated gene transfer and expression in host cell for recombinant vaccine and HIV virus infection therapy WEISSENHORN W; WILEY D; MANTIS N; NEUTRA M R; KOZLOWSKI P ΑU 2003-07165 BIOTECHDS AN WO 2002081655 17 Oct 2002 PΙ ANSWER 42 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New PRO842 polypeptides having structural homology to interleukin-8, TI useful for treating or diagnosing a mammal with an inflammatory disease or immune related disease, e.g. rheumatoid arthritis, osteoarthritis or allergic disease; vector-mediated gene transfer and expression in host cell for recombinant protein production, drug

screening and gene therapy

AU FRENCH D; GRIMALDI J C; HILIAN K J; PISABARRO M T; SCHMIDT K N; SMITH V;

TUMAS D; VANDLEN R L; WATANABE C K; WILLIAMS P M; WOOD W I

AN 2003-05386 BIOTECHDS

PI WO 2002070706 12 Sep 2002

L145 ANSWER 43 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New product comprising a dendroaspin scaffold and a serine protease TI inhibitor domain ligated to the dendroaspin scaffold, useful for treating or preventing diseases associated with thrombosis, e.g. myocardial infarction, stroke; dendroaspin scaffold, serine protease-inhibitor domain and vector expression in host cell use in disease therapy and drug screening ΑU LU X: KAKKAR V V 2003-02235 BIOTECHDS AN WO 2002063017 15 Aug 2002 PΙ ANSWER 44 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 TI Novel lipase variant with reduced potential for odor generation for use in detergent compositions, comprises a parent polypeptide having lipase activity and a peptide extension attached to carboxy terminal of the polypeptide; recombinant protein production via plasmid expression in host cell for surfactant composition ΑU MUNK S; VIND J; BORCH K; PATKAR S A; GLAD S O S; SVENDSEN A AN 2003-03908 BIOTECHDS WO 2002062973 15 Aug 2002 PΙ L145 ANSWER 45 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New human PRO21074 polypeptide, useful for diagnosing, preventing, TT treating or monitoring the progression of cartilaginous disorders, e.g. spondyloarthropathies, rheumatoid arthritis or osteoarthritis; vector-mediated recombinant protein gene transfer and expression in Chinese hamster ovary, Escherichia coli or yeast cell culture for use in disease diagnosis, prevention, therapy and gene therapy ΔII FILVAROFF E; GODDARD A; GRIMALDI J C; WOOD W I 2003-02755 BIOTECHDS AN WO 2002059308 1 Aug 2002 PΙ L145 ANSWER 46 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel human secreted proteins and polynucleotides, useful for diagnosing TI and treating tumors, cardiovascular or endothelial disorders, atherosclerosis, cardiac hypertrophy, angiogenic disorders and bone disorders; vector-mediated recombinant protein gene transfer and expression in host cell for use in gene therapy, recombinant vaccine and nucleic acid vaccine preparation BASINSKI M B; MICANOVIC R; MILLS B J; SANKHAVARAM P R; SU E W; TSCHANG S ΑU R; VARGA G; WANG H 2002-18312 BIOTECHDS AN WO 2002048361 20 Jun 2002 PΤ ANSWER 47 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel ubiquitin conjugating enzyme polypeptide isolated from activated TI human T cell, for screening modulators useful for treating cancer, immune disorder, lymphoproliferative disorder, neurodegenerative disorder; vector-mediated gene transfer, expression in host cell, DNA probe and antibody for recombinant protein production, drug screening and disease therapy BOWEN M A; WU Y; YANG W; FINGER J N ΑU 2002-17873 BIOTECHDS AN WO 2002036741 10 May 2002 ΡI L145 ANSWER 48 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel chemokine-2 polypeptide and polynucleotide encoding the TIpolypeptide, useful for enhancing immune response to an immunogen in a fish:

vector-mediated recombinant oncogene or cytokine fusion

protein gene transfer and expression in host cell

for disease recombinant vaccine, prognosis, diagnosis and gene therapy
AU SUNDICK R S; LIU L; DIXON B; FUJIKI K
AN 2002-18256 BIOTECHDS
PI WO 2002036070 10 May 2002

L145 ANSWER 49 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Novel proteins and polynucleotides of secreted proteins useful for
treating various diseases e.g. rheumatoid arthritis, cancer, psoriasis,
diabetic retinopathy, arteriosclerosis, ischemia or reperfusion injury;
recombinant protein production and sense

and antisense gene use in disease therapy and gene therapy

AU SUEW; WANGH

AN 2002-17830 BIOTECHDS

PI WO 2002026801 4 Apr 2002

L145 ANSWER 50 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Polynucleotide sequences encoding human secretory proteins useful for
gene therapy of e.g. genetic deficiency disorders, cancers, and diseases
caused by intracellular parasites;

recombinant protein gene production via plasmid expression in host cell, sense, antisense, agonist, antagonist, transgenic animal, antibody, cell culture, DNA array and polymerase chain reaction useful in disease gene therapy and drug screening

AU STUART J; LINCOLN S E; ALTUS C M; DUFOUR G E; CHALUP M S; HILLMAN J L; JONES A L; YU J Y; WRIGHT R J; GIETZEN D; LIU T F; YAP P E; DAHL C R; MOMIYAMA M G; BRADLEY D L; ROHATGI S D; HARRIS B; ROSEBERRY A M; GERSTIN E H; PERALTA C H; DAVID M H; PANZER S R; FLORES V; DAFFO A; MARWAHA R; CHEN A J; CHANG S C; AU A P; INMAN R R

AN 2002-12753 BIOTECHDS

PI WO 2002020756 14 Mar 2002

L145 ANSWER 51 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Identifying targeting peptides useful for treating e.g. diabetes
mellitus, inflammatory diseases, cancer, or autoimmune diseases,
comprises exposing a sample to a phage display library and recovering
phage bound to the sample;

adeno-associated virus vector-mediated **recombinant protein** gene transfer and **expression** in host cell,
Fab and humanized antibody for use in prostate cancer, Hodgkin disease, diabetes mellitus, inflammatory disease, arthritis, atherosclerosis, autoimmune disease, bacterium infection, virus infection, cardiovascular disease and neurodegenerative disease diagnosis, therapy and gene therapy

AU ARAP W; PASQUALINI R

AN 2002-13525 BIOTECHDS

PI WO 2002020722 14 Mar 2002

L145 ANSWER 52 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

Monitoring 158P1H4 gene products in biological sample from patient who
has or is suspected of having cancer, useful for treating cancer,
comprises identifying presence of aberrant 158P1H4 gene products in
biological sample;

recombinant protein and monoclonal antibody
production, useful for tumor recombinant vaccine, diagnosis
and prognosis

AU CHALLITA-EID P M; HUBERT R S; RAITANO A B; AFAR D E H; LEVIN E; FARIS M; GE W; JAKOBOVITS A

AN 2002-12096 BIOTECHDS

PI WO 2002016598 28 Feb 2002

L145 ANSWER 53 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

Novel polypeptides and polynucleotides of secreted proteins useful for treating various diseases such as multiple sclerosis, cancer, autoimmune diseases, osteoporosis, Alzheimer's disease and Parkinson's disease;

plasmid pQE60-mediated recombinant IgG Fc region chimeric fusion protein gene transfer and expression in Escherichia coli for disease or disorder diagnosis and gene therapy

EDMONDS B T; MICANOVIC R; OU W; SU E W; TSCHANG S R; WANG H ΑU

ΑN 2002-12425 BIOTECHDS

PΙ WO 2002014358 21 Feb 2002

ANSWER 54 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Polymer based intracellular delivery system for protein phosphatases TI useful for intracellular delivery of protein phosphatases for tumor therapy;

plasmid pET28b vector-mediated recombinant protein gene transfer and expression in Escherichia coli for hydroxypropyl methacrylamide copolymer-PP2C conjugate construction for tumor diagnosis and therapy

ΑU LAVI S; SATCHI-FAINARO R

AN 2002-13518 BIOTECHDS

PΙ WO 2002007670 31 Jan 2002

ANSWER 55 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN 1.145 New purified human S-acyl fatty acid synthase thioesterase-like enzyme, TΙ useful for identifying modulators of enzyme activity for treating cardiovascular disease, diabetes, obesity and hyperlipidemia;

> recombinant protein gene production via plasmid expression in host cell useful in gene therapy

ΑU Y OAIX

AN 2002-06197 BIOTECHDS

PΙ WO 2002000855 3 Jan 2002

1.145 ANSWER 56 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN TI New isolated IL-17 nucleic acids and polypeptides, useful for diagnosing and treating disorders with aberrant expression or activity of the IL-17 polypeptide, such as degenerative cartilaginous and immune-related disorders;

## recombinant protein production and

antagonist and agonist for use in disease therapy and gene therapy ΑU CHEN J; FILVAROFF E; FONG S; FRENCH D; GODDARD A; GODOWSKI P J; GRIMALDI J C; GURNEY A L; HILLAN K J; HYMOWITZ S G; LI H; PAN J; STAROVASNIK M A; TUMAS D; VAN LOOKEREN M; VANDLEN R; WATANABE C K; WILLIAMS P M; WOOD W I; YANSURA D G

2003-22452 BIOTECHDS AN

US 2002182673 5 Dec 2002 PΙ

ANSWER 57 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 New isolated PAL-18 polypeptide, useful for diagnosing, characterizing, ΤI and treating disease and in determining disease susceptibility;

vector-mediated recombinant protein gene transfer and expression in host cell for use in mamma cancer diagnosis and therapy

KINDERS R J; COREY M J AU

2003-03761 BIOTECHDS AN

US 2002106765 8 Aug 2002 PΙ

ANSWER 58 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel isolated Apo-2DcR polypeptide useful for modulating apoptosis in TImammalian cells;

> plasmid pRK5-mediated recombinant protein gene transfer and expression in CHO cell, yeast, Escherichia coli, 293 cell and HeLa cell and hybridoma cell culture for monoclonal antibody production

ΑU ASHKENAZI A J; BAKER K P; CHUNTHARAPAI A; GURNEY A; KIM K J; WOOD W I

2003-03758 BIOTECHDS AN

PΙ US 2002102706 1 Aug 2002 L145 ANSWER 59 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel Nodal and Lefty polypeptides useful for diagnosing or treating cell TT growth and differentiation related disorders in humans, e.g. cancer, autoimmunity, arthritis and immunosuppression; recombinant protein production and sense and antisense sequence use in gene therapy EBNER R; SOPPET D R; RUBEN S M ΔIJ 2003-02695 BIOTECHDS AN PΙ US 2002086351 4 Jul 2002 ANSWER 60 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 Novel antibody specific for a peptide immunogen and comprising at least TI one streptolysin S epitope, useful as vaccinating agent for eliciting an immune response against streptococcal infections; vector-mediated recombinant protein gene transfer and expression in host cell for use in recombinant vaccine preparation and Streptococcus sp. infection prevention and therapy ΑU DALE J B 2003-06510 BIOTECHDS ΔN PΙ US 2002086023 4 Jul 2002 L145 ANSWER 61 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Novel apoprotein antigens encoded by Mycoplasma hyopneumoniae for use in vaccines to prevent and treat diseases caused by infection with Mycoplasma hyopneumoniae in animals, especially pigs; recombinant protein production and sense and antisense sequence use in gene therapy KING K W; MADURA R A; ROSEY E L ΑU 2003-04532 BIOTECHDS AN PΙ EP 1245677 2 Oct 2002 ANSWER 62 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145 New protein immobilized at solid phase by binding site, useful for TT detecting antibodies, comprises multiple antigen/epitope sequences for antibodies, spaced by bridge compositions so that they are exposed for antibody binding; recombinant protein production and immobilization, vector expression in host cell for antibody detection and virus infection testing REPKE H; BUDDE E; NICOLAUS S AU AN 2003-01093 BIOTECHDS EP 1229044 7 Aug 2002 PΙ L145 ANSWER 63 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New cysD, N, K, E and H genes from coryneform bacteria, useful, when over TΤ expressed, for increasing fermentative production of L-amino acids; vector plasmid pEC-XK99E-mediated recombinant protein gene transfer and expression in Escherichia coli for use in L-amino acid preparation and medicine, pharmaceutical and food industries FARWICK M; HUTHMACHER K; PFEFFERLE W; SCHISCHKA N; BATHE B ΑU AN 2002-16465 BIOTECHDS DE 10136986 21 Mar 2002 PΙ L145 ANSWER 64 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN Cloning, characterization and biotechnological use of Physcomitrella patens proteins and enzymes involved in the synthesis of amino acids, vitamins, cofactors, nucleotides and nucleosides SO U.S. Pat. Appl. Publ., 107 pp. CODEN: USXXCO Lerchl, Jens; Renz, Andreas; Ehrhardt, Thomas; Reindl, Andreas; Cirpus, IN Petra; Bischoff, Friedrich; Frank, Markus; Freund, Annette; Duwenig, Elke; Schmidt, Ralf-Michael; Reski, Ralf 2002:755097 HCAPLUS AN DN 137:275028

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
PI	US 2002142422	A1	20021003	US 2000-734017	20001212		
L145 TI		Chlamy	domonas rei	HT 2006 Elsevier Scienc nhardtii reveal transcr ine biosynthesis			
so				/4 (2076-2084), 47 refe	rence(s)		
	CODEN: PLPHAY ISS						
AU	Ravina C.G.; Chang	r CI.;	– Tsakraklide	es G.P.; McDermott J.P.	; Vega J.M.;		

- AN 2002:36035203 BIOTECHNO
- L145 ANSWER 66 OF 199 MEDLINE on STN

Leustek T.; Gotor C.; Davies J.P.

- TI Limits to sulfur accumulation in transgenic lupin seeds expressing a foreign sulfur-rich protein.
- SO Plant physiology, (2002 Mar) Vol. 128, No. 3, pp. 1137-48. Journal code: 0401224. ISSN: 0032-0889.
- AU Tabe Linda M; Droux Michel
- AN 2002160076 MEDLINE
- L145 ANSWER 67 OF 199 MEDLINE on STN DUPLICATE 4
- TI Removal of DnaK contamination during fusion protein purifications.
- SO Protein expression and purification, (2002 Aug) Vol. 25, No. 3, pp. 503-7. Journal code: 9101496. ISSN: 1046-5928.
- AU Rial Daniela V; Ceccarelli Eduardo A
- AN 2002489079 MEDLINE
- L145 ANSWER 68 OF 199 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
- TI Recombinant human CIS2 (SOCS2) protein: Subcloning, expression, purification, and characterization.
- SO Protein Expression and Purification, (July, 2002) Vol. 25, No. 2, pp. 305-312. print.

  CODEN: PEXPEJ. ISSN: 1046-5928.
- AU Biener, Eva; Maurice, Sarah; Sandowski, Yael; Cohen, Yael; Gusakowsky, Eugene E.; Hooghe, Robert; Yoshimura, Akihiko; Livnah, Oded; Gertler, Arieh [Reprint author]
- AN 2002:502157 BIOSIS
- L145 ANSWER 69 OF 199 LIFESCI COPYRIGHT 2006 CSA on STN
- TI Secretory production of recombinant human C-reactive protein in Escherichia coli , capable of binding with phosphorylcholine, and its characterization
- SO Biochemical and Biophysical Research Communications [Biochem. Biophys. Res. Commun.], (20020705) vol. 295, no. 1, pp. 163-166.
  ISSN: 0006-291X.
- AU Tanaka, T.; Horio, T.; Matuo, Y.
- AN 2002:103909 LIFESCI
- L145 ANSWER 70 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
- TI Cloning and characterization of an insecticidal crystal protein gene from Bacillus thuringiensis subspecies kenyae
- SO Journal of Genetics (2002), 81(1), 5-11 CODEN: JOGNAU; ISSN: 0022-1333
- AU Misra, Hari S.; Khairnar, Nivedita P.; Mathur, Manjula; Vijayalakshmi, N.; Hire, Ramesh S.; Dongre, T. K.; Mahajan, S. K.
- AN 2002:773523 HCAPLUS
- DN 138:131850
- L145 ANSWER 71 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
- TI Isolated PRO1356, PRO617, PRO1030, PRO4302 polypeptides, useful for treating immune disorders such as thyroiditis, diabetes mellitus, allergic disease, asthma, allergic rhinitis, atopic dermatitis; retro virus vector-mediated recombinant protein

```
gene transfer and expression in CHO cell, Escherichia
         coli and yeast, antagonist, agonist, antisense, DNA primer,
         DNA probe, monoclonal antibody, humanized antibody, singlechain
         antibody, expressed sequence tag, database and bioinformatic software
         for disease diagnosis and gene therapy
      EATON D L; FONG S; GODDARD A; GODOWSKI P J; GRIMALDI C J; GURNEY A L;
ΑU
      WATANABE C K; WOOD W I; ZHANG Z
AN
      2002-06124 BIOTECHDS
      WO 2001092331 6 Dec 2001
ΡI
      ANSWER 72 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L145
      Novel subtilisin protease variants useful in cleaning
TI
      compositions, e.g. laundry compositions and personal
      care compositions, has amino acid deletions
      in defined epitope regions;
         phagemid-mediated gene transfer, expression in Bacillus
         subtilis and site-specific mutagenesis for recombinant
         protein production and cleaner surfactant
AU
      Rubingh D N; Sikorski E E
      2001-06294 BIOTECHDS
AN
PΙ
      WO 2001007575 1 Feb 2001
      ANSWER 73 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L145
      New fertile transgenic maize plant comprises amino acid-elevating amount
ΤI
      of expressed recombinant inheritable gene encoding
      seed storage protein;
         plasmid ppHYGI1, plasmid pBII221 and plasmid pZ27Z10-mediated
         Escherichia coli beta-glucuronidase gene transfer and
         expression in maize transgenic plant for improved herbicide resistance
ΑU
      Lundquist R C; Walters D A; Kirihara J A
AN
      2002-03070 BIOTECHDS
PΙ
      US 2001032344 18 Oct 2001
      ANSWER 74 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
      Composition comprising mutant immunoglobulin (Ig)G molecule having
TΙ
      increased half-life relative to IqG, decreasing endogenous serum IqG in a
      subject, comprises amino acid substitutions in Fc-hinge fragment;
         vector-mediated gene transfer, expression in host cell and
         site-directed mutagenesis for recombinant protein
         production, vaccine and immunotherapy
AII
      WARD E S
      2002-12089 BIOTECHDS
AN
      US 6277375 21 Aug 2001
PT
      ANSWER 75 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L145
      Novel rhesus receptor having affinity for neuropeptide-Y, pancreatic
      peptide-P or peptide-YY is useful for identifying compounds for treating
      disorders and diseases which include cardiovascular conditions and
      cerebral disorders;
         vector-mediated gene transfer, expression in Escherichia
         coli or mammal host cell for recombinant
         protein production, drug screening and disease
         therapy or prevention
AU
      Baez M; Yang P
AN
      2001-12439 BIOTECHDS
PΙ
      US 6242251 5 Jun 2001
L145
     ANSWER 76 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
      Novel mammalan genes encoding cytokine synthesis inhibitory factor
      (IL-10) and pharmaceutical compositions containing them for treating
      diseases associated with cytokine imbalance;
         plasmid pcD(SR-a)-mediated interleukin-10 gene transfer and
         expression in COS-7 cell for recombinant
         protein production and disease therapy
ΑU
      Mosmann T R; Moore K W; Bond M W; Vieira P J M
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AN
     2001-09374 BIOTECHDS
ΡI
     US 6217857 17 Apr 2001
L145 ANSWER 77 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
     Human G protein-coupled receptors and their cDNA sequences and tissue
ΤI
     expression profiles
SO
     PCT Int. Appl., 193 pp.
     CODEN: PIXXD2
IN
     Parodi, Luis A.; Lind, Peter; Sejlitz, Torsten
     2001:816733 HCAPLUS
AN
DN
     135:353834
                                         APPLICATION NO. DATE
     PATENT NO.
                       KIND
                               DATE
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                                          ______
                                                                 -----
                                        WO 2001-US14050
PΙ
    WO 2001083553
                        A2
                               20011108
                                                                 20010501
                               20020822
     WO 2001083553
                        A3
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        W:
            CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
            HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
            RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
            VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                        AU 2001-59322
     AU 2001059322
                         A5
                               20011112
                               20030129
                                         EP 2001-932827
    EP 1278844
                         A2
                                                                 20010501
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
L145 ANSWER 78 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
TT
    Human G protein-coupled receptors and their cDNA sequences and tissue
     expression profiles
SO
     PCT Int. Appl., 189 pp.
     CODEN: PIXXD2
    Vogeli, Gabriel
IN
     2001:763192 HCAPLUS
AN
DN
     135:299596
                                        APPLICATION NO.
    PATENT NO.
                       KIND DATE
                                                               DATE
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                       _ _ _ _
                               20011018
                                         WO 2001-US11330
                                                                20010406
PΙ
    WO 2001077330
                        A2
                               20030206
    WO 2001077330
                        A3
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
            HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
            RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
            VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
    AU 2001049922
                               20011023
                                        AU 2001-49922
                                                                 20010406
                         Α5
                                         US 2001-828644
                               20020207
                                                                 20010406
    US 2002015998
                         A1
                                        EP 2001-923209
    EP 1303601
                         A2
                               20030423
                                                                 20010406
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
L145 ANSWER 79 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
    Recombinant production of active protein in
    prokaryotes by refolding with reducing agent in arginine containing
    solution
SO
    PCT Int. Appl., 57 pp.
    CODEN: PIXXD2
    Yamada, Takao; Tsuji, Isamu; Matsui, Hideki
IN
    2001:747994 HCAPLUS
AN
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DN

135:300248

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KIND
                               DATE
                                         APPLICATION NO.
                                                                  DATE
     PATENT NO.
                             -----
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                                          ______
                               20011011 WO 2001-JP2712 20010330
PΤ
     WO 2001075095
                        A1
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
            HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT,
            LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
            SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
            YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                         AA
                               20011011 CA 2001-2404567
                                                                  20010330
     CA 2404567
                                        AU 2001-44647
     AU 2001044647
                         A5
                               20011015
                                                                  20010330
     JP 2001342198
                        A2
                               20011211
                                        JP 2001-99706
                                                                  20010330
                               20030108
                                        EP 2001-917667
    EP 1273655
                         A1
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2003120042
                               20030626
                                          US 2002-240295
                                                                  20020927
                         A1
L145 ANSWER 80 OF 199 LIFESCI
                                 COPYRIGHT 2006 CSA on STN
     Characterization of the Enzymatic Component of the ADP-Ribosyltransferase
     Toxin CDTa from Clostridium difficile
     Infection and Immunity [Infect. Immun.], (20011000) vol. 69, no. 10, pp.
SO
     6004-6011.
     ISSN: 0019-9567.
     Guelke, I.; Pfeifer, G.; Liese, J.; Fritz, M.; Hofmann, F.; Aktories, K.;
AU
     Barth, H.*
     2001:110094 LIFESCI
AN
     ANSWER 81 OF 199 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
1.145
     Production of β-(pyrazol-1-yl)-L-alanine from L-serine and pyrazol
TΤ
      using recombinant Escherichia coli cells expressing serine
      acetyltransferase and O-acetylserine sulfhydrylase-A
      Biotechnology Letters, (2001), 23/24 (2051-2055), 11 reference(s)
SO
      CODEN: BILED3 ISSN: 0141-5492
ΑU
     Mino K.; Yamanoue T.; Ohno K.; Sakiyama T.; Eisaki N.; Matsuyama A.;
     Nakanishi K.
      2001:34073241
                     BIOTECHNO
AN
L145 ANSWER 82 OF 199
                         MEDLINE on STN
                                                       DUPLICATE 5
     cDNA cloning and molecular identification of the major oyster allergen
ΤI
     from the Pacific oyster Crassostrea gigas.
     Clinical and experimental allergy : journal of the British Society for
so
     Allergy and Clinical Immunology, (2001 Aug) Vol. 31, No. 8, pp. 1287-94.
     Journal code: 8906443. ISSN: 0954-7894.
ΑU
     Leung P S; Chu K H
     2001487002
                   MEDLINE
ΑN
                                 COPYRIGHT 2006 CSA on STN
L145 ANSWER 83 OF 199 LIFESCI
    Rapid Isolation of Monoclonal Antibodies. Monitoring Enzymes in the
ΤI
     Phytochelatin Synthesis Pathway
     Plant Physiology [Plant Physiol.], (20011100) vol. 127, no. 3, pp.
SO
     711-719.
     ISSN: 0032-0889.
     Li, Y.; Kandasamy, M.K.; Meagher*, R.B.
AU
     2002:8776 LIFESCI
AN
L145 ANSWER 84 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
     Potentiating immune responses to antigens using specified Mycobacterium
TI
      tuberculosis proteins;
```

recombinant protein production for interleukin-12 and interferon-gamma

AU

AN

Skeiky Y

2000-12157 BIOTECHDS

ANSWER 85 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN L145

New polynucleotides encoding proteins, with e.g. nutritional, chemokine, ΤI immune stimulating or suppressing, hematopoiesis regulating, tissue growth, tumor inhibition or antiinflammatory activity;

human brain, kidney, blood, bladder, etc. recombinant protein production via vector-mediated gene transfer and expression in mammal host cell for disease therapy

Jacobs K; McCoy J M; LaVallie E R; Collins-Racie L A; Evans C; Merberg D; ΑU Treacy M; Agostino M J; Steininger II R J; Spaulding V; Wong G G; Clark H F; Fechtel K

AN 2000-06517 BIOTECHDS

WO 2000009552 24 Feb 2000 PΙ

ANSWER 86 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN New polynucleotides encoding human retinoid binding protein especially useful for diagnosing, treating and preventing cancer, inflammation and disorders associated with retinoid metabolism;

recombinant protein production via

vector plasmid pBluescript-mediated gene transfer and expression in Escherichia coli for diagnosis, therapy and gene therapy

ΑU Bandman O; Guegler K J; Shah P

AN 2000-07809 BIOTECHDS

PΙ US 6046027 4 Apr 2000

L145 ANSWER 87 OF 199 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

An isolated polypeptide conserved in proteobacterial extracellular domains used in the treatment and prevention of bacterial infections.

PΤ A1 20001019 (200062)\* EN 83 A61K038-00 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE W: JP US

LUPAS, A N IN

L145 ANSWER 88 OF 199 MEDLINE on STN DUPLICATE 6

Characterization of O-acetyl-L-serine sulfhydrylase purified from an alkaliphilic bacterium.

Bioscience, biotechnology, and biochemistry, (2000 Nov) Vol. 64, No. 11, SO pp. 2352-9. Journal code: 9205717. ISSN: 0916-8451.

Sugihara Y; Yamagata S; Mizuno Y; Ezaki T AU

2001138968 MEDLINE ΑN

L145 ANSWER 89 OF 199 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on DUPLICATE 7

TI Recombinant decorsin: Dynamics of the RGD recognition site.

SO Protein Science, (August, 2000) Vol. 9, No. 8, pp. 1428-1438. print. ISSN: 0961-8368.

Krezel, Andrzej M. [Reprint author]; Ulmer, Jana S.; Wagner, Gerhard; AU Lazarus, Robert A.

2000:424640 BIOSIS AN

L145 ANSWER 90 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN

Cloning and recombinant expression of insulin receptor ligand-binding TI domains

Shengwu Huaxue Yu Shengwu Wuli Xuebao (2000), 32(6), 627-632 SO CODEN: SHWPAU; ISSN: 0582-9879

Zhang, Hong; Qiao, Zhi-Song; Feng, You-Min AU

2001:3783 HCAPLUS AN

135:205742 DN

L145 ANSWER 91 OF 199 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN

Expression of a bacterial serine acetyltransferase in transgenic potato plants leads to increased levels of cysteine

- and glutathione
- SO Plant Journal, (2000), 22/4 (335-343), 54 reference(s) CODEN: PLJUED ISSN: 0960-7412
- AU Harms K.; Von Ballmoos P.; Brunold C.; Hofgen R.; Hesse H.
- AN 2000:30400021 BIOTECHNO
- L145 ANSWER 92 OF 199 MEDLINE on STN DUPLICATE 8
- TI Molecular cloning and functional characterization of cDNAs encoding cysteine synthase and serine acetyltransferase that may be responsible for high cellular cysteine content in Allium tuberosum.
- SO Gene, (2000 Oct 31) Vol. 257, No. 2, pp. 269-77. Journal code: 7706761. ISSN: 0378-1119.
- AU Urano Y; Manabe T; Noji M; Saito K
- AN 2001061875 MEDLINE
- L145 ANSWER 93 OF 199 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
- TI Regulation of sulfate transport and synthesis of sulfur-containing amino acids
- SO CURRENT OPINION IN PLANT BIOLOGY, (JUN 2000) Vol. 3, No. 3, pp. 188-195. ISSN: 1369-5266.
- AU Saito K (Reprint)
- AN 2000:377187 SCISEARCH
- L145 ANSWER 94 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
- TI Extracellular Expression, Purification, and Characterization of a Winter Flounder Antifreeze Polypeptide from Escherichia coli
- SO Protein Expression and Purification (2000), 18(2), 175-181 CODEN: PEXPEJ; ISSN: 1046-5928
- AU Tong, Li; Lin, Qingsong; Wong, W. K. Raymond; Ali, Asma; Lim, Daniel; Sung, Wing L.; Hew, Choy L.; Yang, Daniel S. C.
- AN 2000:127507 HCAPLUS
- DN 132:344551
- L145 ANSWER 95 OF 199 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 9
- TI Characterization of Api g 1.0201, a new member of the Api g 1 family of celery allergens.
- SO International Archives of Allergy and Immunology, (2000) Vol. 122, No. 2, pp. 115-123. .
  Refs: 49
  - ISSN: 1018-2438 CODEN: IAAIEG
- AU Hoffmann-Sommergruber K.; Ferris R.; Pec M.; Radauer C.; O'Riordain G.; Laimer da Camara Machado M.; Scheiner O.; Breiteneder H.
- AN 2000238357 EMBASE
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		W:	AU,	CA,	FI,	JP,	NO.	, US								
		RW:	ΑT,	BE,	CH,	DE,	DK,	, ES,	FR,	GB, G	R, IT,	LU,	NL,	SE		
	AT	9001	685			A		1995	1115	PΑ	1990-	1685			1	9900813
	ΑT	4011	80			В		1996	0725							
	CA	2067	182			AA		1992	0214	CA	1991-	20671	82		1	9910809
	ΑŲ	9183	901			A1		1992	0317	AU	1991-	83901			1	9910809
	ΑU	6596	09			B2		1995	0525							
	ΕP	4950	64			A1		1992	0722	EP	1991-	91458	1		1	9910809
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ΑT	203055	Е	20010715	AT	1991-914581	19910809
NO	9201375	Α	19920612	NO	1992-1375	19920408
NO	304189	B1	19981109			
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		B1 19960320			
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	W: AU, BG, DK,	FI, JP, KR, NO,	RO, SU, US		
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	JP 03501323	T2 19910328	JP 1988-507383	19880913	
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L145 ANSWER 199 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN
    Biosynthesis of cysteine from serine and hydrogen sulfide
ΤI
    Biochemische Zeitschrift (1957), 328, 591-4
so
    CODEN: BIZEA2; ISSN: 0366-0753
     Schlossmann, Klaus; Lynen, Feodor
ΑU
     1957:62619 HCAPLUS
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    51:62619
OREF 51:11414f-g
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=> d ab 29,64,68-70,81,94,101,105-107,110,114,119,127,128,132,136,137,149
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MEDLINE on STN

Variations in proteome **profiles** of Escherichia **coli** in response to the overproduction of human leptin, a **serine**-

DUPLICATE 1

L145 ANSWER 29 OF 199

rich (11.6% of total amino acids) protein, were examined by two-dimensional gel electrophoresis. The levels of heat shock proteins increased, while those of protein elongation factors, 30S ribosomal protein, and some enzymes involved in amino acid biosynthesis decreased, after leptin overproduction. Most notably, the levels of enzymes involved in the biosynthesis of serine family amino acids significantly decreased. Based on this information, we designed a strategy to enhance the leptin productivity by manipulating the cysK gene, encoding cysteine synthase A. By coexpression of the cysK gene, we were able to increase the cell growth rate by approximately twofold. Also, the specific leptin productivity could be increased by fourfold. In addition, we found that cysK coexpression can improve the production of another serine-rich protein, interleukin-12 beta chain, suggesting that this strategy may be useful for the production of other serine-rich proteins as well. The approach taken in this study should be useful in designing a strategy for improving recombinant protein production.

- L145 ANSWER 64 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN

  AB Isolated nucleic acid mols., designated metabolic pathway protein (MP) nucleic acid mols., which encode novel MP proteins from Phycomitrella patens are are described. The cDNA sequences and the encoded amino acid sequences of a number of MP enzymes and proteins are disclosed. The invention also provides antisense nucleic acid mols., recombinant expression vectors containing MP protein nucleic acid mols., and host cells into which the expression vectors have been introduced. The invention still further provides isolated MP proteins, mutated MP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from transformed cells, organisms or plants based on genetic engineering of MP protein genes in these organisms.
- L145 ANSWER 68 OF 199 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
- The 1x myc-tagged cDNA encoding for human CIS2 protein was subcloned into a pET-29a+ vector in order to express and produce a recombinant S-peptide tagged and 1x myc-tagged protein in Escherichia coli BL21(DE3). The constitutively expressed protein was isolated from inclusion bodies by a simple solubilization-renaturation procedure and purified by anion-exchange chromatography on Q-Sepharose. The recombinant form was found to be pure and monomeric as judged by both SDS-PAGE and gel-filtration chromatography and its biological activity was proven by its ability to bind to the tyrosine-phosphorylated cytosolic fragment of human growth hormone receptor fused to glutathione-S-transferase. Recombinant CIS2 was compared by biochemical, immunological, and molecular methods to the CIS2 protein expressed in eukaryotic cells. This report describes the first substantial production of biologically active recombinant human CIS2.
- L145 ANSWER 69 OF 199 LIFESCI COPYRIGHT 2006 CSA on STN

  AB Recombinant human CRP (rhCRP) was secreted into culture supernatant of Escherichia coli by co-expressing kil gene that has a function to secrete colicin E1 outside the cell. Highly purified 5 g rhCRP was produced from 180 L culture supernatant by affinity chromatography. The purified rhCRP was indistinguishable from the native one with respect to Ca super(2+) -dependent binding ability to phosphorylcholine, electrophoretic behavior, N-terminal amino acid analysis, and immunochemical properties. The molecular weight of rhCRP monomer was determined to be 23059.7 Da by TOF/MS analysis. These results indicate that rhCRP has the same protein structure as native one and that rhCRP has the potential as a reference material and/or calibrator of high-sensitivity CRP assay to predict the risk of cardiovascular disease. [copy ] 2002 Elsevier Science (USA)

- L145 ANSWER 70 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN A sporulating culture of Bacillus thuringiensis subsp. kenyae strain HD549 is toxic to larvae of lepidopteran insect species such as Spodoptera litura, Helicoverpa armigera and Phthorimaea operculella, and a dipteran insect, Culex fatigans. A 1.9-kb DNA fragment, PCR-amplified from HD549 using cryll-gene-specific primers, was cloned and expressed in E. coli. The recombinant protein produced 92% mortality in first-instar larvae of Spodoptera litura and 86% inhibition of adult emergence in Phthorimaea operculella, but showed very low toxicity against Helicoverpa armigera, and lower mortality against third-instar larvae of dipteran insects Culex fatigans, Anopheles stephensi and Aedes aegypti. The sequence of the cloned crystal protein gene showed almost complete homol. with a mosquitocidal toxin gene from Bacillus thuringiensis var. kurstaki, with only five mutations scattered in different regions. Amino acid alignment with different insecticidal crystal proteins using the MUTALIN program suggested presence of the conserved block 3 region in the sequence of this protein. A mutation in codon 409 of this gene that changes a highly conserved phenylalanine residue to serine lies in this block.
- L145 ANSWER 81 OF 199 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN  $\beta$ -(Pyrazol-1-yl)-L-alanine ( $\beta$ -PA) was produced from L-serine and pyrazol using recombinant Escherichia coli cells expressing serine acetyltransferase and O-acetylserine sulfhydrylase-A. The amount of  $\beta$ -PA increased with increasing L-serine concentrations up to 600 mM at 50 mM pyrazol while 100 mM pyrazol gave the highest  $\beta$ -PA production with 50 mM L-serine. Under the optimized conditions,  $\beta$ -PA accumulated in the broth at approximately 140 mM with a conversion of 90% with respect to the added amount of pyrazol.
- L145 ANSWER 94 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN HPLC6 is the major component of liver-type antifreeze polypeptides (AFPs) from the winter flounder, Pleuronectes americanus. To facilitate mutagenesis studies of this protein, a gene encoding the 37-amino acid mature polypeptide was chemical synthesized and cloned into the Tac cassette immediately after the bacterial ompA leader sequence for direct excretion of the AFP into the culture medium. Escherichia coli transformant with the construct placIQpar8AF was cultured in M9 medium. The recombinant AFP (rAFP) was detected by a competitive ELISA. After IPTG induction, a biol. active rAFP was expressed. The majority of the rAFP was excreted into the culture medium with only trace amts. trapped in the periplasmic space and cytoplasm. After 18 h of induction, the accumulated rAFP in the culture medium amounted to about 16 mg/L. excreted AFP was purified from the culture medium by a single-step reverse-phase HPLC. Mass spectrometric and amino acid composition analyses confirmed the identity of the purified product. The rAFP, which lacked amidation at the C-terminal, was about 70% active when compared to the amidated wild-type protein, thus confirming the importance of C-terminal cap structure in protein stability and function. (c) 2000 Academic Press.
- L145 ANSWER 101 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN

  AB The consensus repeat sequence found in the dragline silk from the spider, Nephila clavipes, was redesigned to incorporate a redox trigger flanking the β-sheet-forming polyalanine sequences. The methionine redox trigger, in the oxidized state, was incorporated to prevent the formation of the β-sheets; in the reduced state it would not result in steric limitations to β-sheet formation. A synthetic gene incorporating the trigger was constructed, cloned, and expressed in Escherichia coli

  . The purified protein, .apprx.25 kDa, contained the expected amino acid composition and migration behavior on SDS-PAGE. The recombinant protein was analyzed by x-ray diffraction, TEM, electron diffraction, and CD in both oxidized and reduced states. Based on the results, the incorporation of a redox trigger appears to be a powerful exptl. strategy to explore the self-assembly of fibrous proteins

such as silks.

- L145 ANSWER 105 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN The combination of 2-D PAGE, computer image anal., and several protein identification techniques allowed the Escherichia coli SWISS-2DPAGE database to be established. This is part of the ExPASy mol. biol. server accessible through the WWW at the URL address http://www.expasy.ch/ch2d/ch2d-top.html. The authors report recent progress in the development of the E. coli SWISS-2DPAGE database. Proteins were separated with immobilized pH gradients in the 1st dimension and Na dodecyl sulfate-polyacrylamide gel electrophoresis in the 2nd dimension. To increase the resolution of the separation and thus the number of identified proteins, a variety of wide and narrow range immobilized pH gradients were used in the 1st dimension. Micropreparative gels were electroblotted onto polyvinylidene difluoride membranes and spots were visualized by amido black staining. Protein identification techniques such as amino acid composition anal., gel comparison and microsequencing were used, as well as a recently described Edman sequence tag approach. Some of the above identification techniques were coupled with database searching tools. Currently 231 polypeptides are identified on the E. coli SWISS-2DPAGE map: 64 were identified by N-terminal microsequencing, 39 by amino acid composition, and 82 by sequence tag. Of 153 proteins putatively identified by gel comparison, 65 were confirmed. Many proteins were identified using more than 1 technique. Faster progress in the E. coli proteome project will now be possible with advances in biochem. methodol. and with the completion of the entire E. coli genome.
- L145 ANSWER 106 OF 199 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 16
- The psoriasis-associated fatty acid binding protein (PA-FABP, also known as FABP5) is a novel keratinocyte protein that is highly up-regulated in psoriatic plaques (P. Madsen, H.H. Rasmussen, H. Leffers, B. Honore and J.E. Celis, J. Invest. Dermatol. 1992, 99, 299-305). Here we have expressed PA-FABP in Escherichia coli as a fusion protein containing an NH2-terminal hexa-His tag followed by a factor Xa cleavage site. The recombinant protein was expressed at a level of about 30% of the soluble proteins and was purified to homogeneity using a simple two-step protocol consisting of affinity chromatography on Ni2+-nitrilotriacetic acid agarose followed by gel filtration. The recombinant protein was then digested with factor Xa and characterized by two-dimensional gel electrophoresis. The ability of PA-FABP to bind saturated fatty acids ranging from 6 to 16 carbons was determined directly by dialysis and compared to human serum albumin (HSA). The results showed that PA-FABP binds multiple molecules of the fatty acids hexanoate (C(6:)), octanoate (C(8:0)), decanoate (C(10:0)) and laurate (C(12:0)), all with a K1 of about 104 M-1, and myristate (C(14:0)) with a K1 of 4.4 X 105 M-1. Palmitate (C(16:)) also bound strongly with multiple molecules. Due to the very low solubility of palmitate its affinity to PA-FABP was measured relatively to HSA and found to be 8.1 times lower. At ligand/protein ratios below 1, all fatty acids bound to PA-FABP with about one to three orders of magnitude lower affinity than to HSA. The difference in the fatty acid binding properties of the two proteins may reflect differences in their three-dimensional structures, which in the case of PA-FABP consists mainly of  $\beta$ -sheets while HSA contains predominantly  $\alpha$ -helices.
- L145 ANSWER 107 OF 199 LIFESCI COPYRIGHT 2006 CSA on STN

  AB Coexpression of di- alpha -globin and beta -globin in Escherichia

  coli in the presence of exogenous heme yielded high levels of
  soluble, functional recombinant human hemoglobin (rHb1.1). High-level
  expression of rHb1.1 provides a good model for measuring
  mistranslation in heterologous proteins. rHb1.1 does
  not contain isoleucine; therefore, any isoleucine present could be
  attributed to mistranslation, most likely mistranslation of one or more of

the 200 codons that differ from an isoleucine codon by 1 bp. Sensitive amino acid analysis of highly purified rHb1.1 typically revealed less than or equal to 0.2 mol of isoleucine per mol of hemoglobin. This corresponds to a translation error rate of less than or equal to 0.001, which is not different from typical translation error rates found for E. coli proteins. Two different expression systems that resulted in accumulation of globin proteins to levels equivalent to similar to 20% of the level of E. coli soluble proteins also resulted in equivalent translational fidelity.

- L145 ANSWER 110 OF 199 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 19
- The amplified expression of a recombinant AB protein is known to lend to an intracellular depletion of specific amino acid pools which in turn may affect the production of the desired protein. In order to counteract and overcome such a situation during the fermentation of the recombinant Escherichia coli (PMSG27) containing the glucose isomerase (GI) gene from Streptomyces sp. NCIM 2730, the effect of addition of different amino acids on the specific activity of GI was studied. The amino acid composition of Gl from Streptomyces sp. NCIM 2730 reveals predominantly aspartic acid glutamic acid, and glycine; therefore, in the present paper; the effect of coordinated addition of the assorted combinations of these three amino acids on the synthesis of recombinant GI was studied. The results were analyzed using a 2(3) factorial design. The following conclusions were derived from the analysis of two-factor interactions of the three amino acids: (i) The interaction between the aspartic and glutamic acid is independent of aspartic acid concentration but is affected by the increasing concentrations of glutamic acid, (ii) The effect of aspartic acid concentration is more than that of glycine, and (iii) During the interaction of glutamic acid and glycine, the effect of glutamic acid is more prominent than that of glycine. The three-factor interaction analyses reveal that the effect of the three amino acids is in the order aspartic acid > glutamic acid > glycine. (C) 1998 Elsevier Science Inc.
- L145 ANSWER 114 OF 199 LIFESCI COPYRIGHT 2006 CSA on STN

  AB Isolation of the recombinant protein from a genetically engineered Escherichia coli 1854 producer for further chemical enzymatic transformation into human insulin through proinsulin was studied. Under optimal conditions, the recombinant protein formation was more than 35% of the total cell proteins. Structures of the polypeptides obtained and purified chromatographically were confirmed by amino acid analysis. Human proinsulin was derived from the recombinant protein isolated.
- L145 ANSWER 119 OF 199 MEDLINE on STN DUPLICATE 24

  AB A partial cDNA clone, from the 3' end of the dragline silk gene was isolated from Nephila clavipes major ampullate glands. This clone contains a 1.7-kb insert, consisting of a repetitive coding region of 1.4-kb and a 0.3-kb nonrepetitive coding region; 1.5-kb of the 1.7-kb fragment was cloned into Escherichia coli and a 43-kDa recombinant silk protein was expressed.

  Characterization of the purified protein by Western blot, amino acid composition analysis, and matrix-assisted laser desorption ionization/time-of-flight mass spectrometry confirms it to be spider dragline silk.
- L145 ANSWER 127 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN

  AB Previous research has shown that overexpression of recombinant proteins places a metabolic burden on the host cell. Anal. shows that recombinant proteins expressed in Escherichia coli at less than 10% of total protein have an average amino acid composition which is rich in amino acids from the aromatic and serine biosynthetic families. A neg. correlation is observed

between expression level and aromatic amino acid and cysteine content relative to the host. We hypothesize that when an amino acid is present in a recombinant protein at levels significantly higher than present in host cellular protein, the amino acid becomes a limiting factor in expression level. Results will be presented which suggest that 1) the amino acid composition of a recombinant protein can affect its expression level, and 2) the metabolic burden imposed by amino acid compn. can be alleviated by supplementing the cell with required precursors, leading to significant increases in recombinant protein expression.

- L145 ANSWER 128 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN Gilthead seabream (S. aurata) insulin-like growth factor-I (gsIGF-I) cDNA coding for the mature protein was cloned in a pGEM-3Z vector, and then transferred into prokaryotic expression vector pET-11a and expressed in E. coli BL21(DE3) cells upon induction with iso-Pr thiogalactoside. The expressed protein contained within the inclusion-body pellet was solubilized in 4.5M urea, refolded for 24 h at pH 11.3 in the presence of catalytic amts. of cysteine, and purified to >98% purity, as a monomeric methionyl-gsIGF-I. Amino acid composition and N-terminal sequence confirmed the identity to be the predicted protein. Binding assays of the 125I-gsIGF-I to gilthead seabream or carp (Cyprinus carpio) sera resulted in high specific binding, indicating the existence of  $\geq 1$  IGF-binding proteins. In binding expts. to crude gilthead seabream brain homogenate, using human (h) IGF-I, as a ligand, the resp. IC50 value of hIGF-I was .apprx.4-fold lower than that of gsIGF-I. Recombinant gsIGF-I exhibited mitogenic activity in a mouse mammary gland-derived MME-L1 cell line which was .apprx.200-fold lower than that of hIGF-I. Binding expts. to intact MME-L1 cells suggests that this difference most likely results from a correspondingly lower affinity for IGF-I receptor in these cells. In contrast, the activities of gsIGF-I and hIGF-I measured by 35S uptake by gill arches from the goldfish (Carassius auratus) were identical, indicating that the recombinant gsIGF-I is biol. active.
- L145 ANSWER 132 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN Previous research has shown that overexpression of recombinant proteins AB places a metabolic burden on the host cell. Analysis shows that recombinant proteins expressed in Escherichia coli at less than 10% of total protein have an average amino acid composition which is rich in amino acids from the aromatic and serine biosynthetic families. A negative correlation was observed between expression level and aromatic amino acid and cysteine content relative to the host. It was hypothesized that when an amino acid is present in a recombinant protein at levels significantly higher than present in host cellular protein, the amino acid becomes a limiting factor in expression level. Results were presented which suggest that the amino acid composition of a recombinant protein can affect its expression level and the metabolic burden imposed by amino acid composition can be alleviated by supplementing the cell with required precursors, leading to significant increases in recombinant protein production (0 ref)
- L145 ANSWER 136 OF 199 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
- AB Fed-batch culture with controlled L-amino acid composition was performed to improve production of a recombinant gene product in Bacillus brevis. The maximum recombinant protein (alpha-amylase) level and specific activity increased from 5.14 kU/mL and 0.77 kU/mg dry cell in conventional fed-batch culture to 12.01 kU/mL and 2.64 kU/mg dry cell, respectively, when L-amino acid concentration was controlled at 5 mM using an asparagine (Asn) and isoleucine

(Ile)-enriched nitrogen source. The L-amino acid concentration in the culture was monitored by an automatic biotech analyzer and controlled at 2-20 mM using a mixture of polypeptone and yeast extract. Although L-amino acid concentrations were controlled at low levels, the alpha-amylase activity increased only 1.3 times compared to an uncontrolled batch culture; accumulation of ammonium ion was not reduced. When L-amino acid was controlled at the high level, more cell mass and less recombinant gene product were produced than in those with low control level. To overcome ammonium ion inhibition, the specific amino acids Asn and lie were substituted to improve the production of gene product. Addition of these amino acids to a flask culture led to an improvement in the enzyme production level and specific activity to 2.9 and 5.1 times, respectively, as high as that without them. Both the control of amino acids at low concentrations and the enrichment of Asn and lie were effective for the improvement of recombinant protein production from recombinant B. brevis cells. (C) 1996 John Wiley & Sons, Inc.

L145 ANSWER 137 OF 199 HCAPLUS COPYRIGHT 2006 ACS on STN

AB Heterologous proteins may be expressed in

bacteria, where protein engineering techniques can be used to alter the amino acid sequence. As the amino acid compn

. of the mol. shifts, it is sometimes possible to identify proteins with augmented properties or to identify domains crucial for biol. function. We have developed expression systems that make it possible to produce recombinant proteins at high yield

from E. coli where partitioning of the product into a cellular compartment can complement a purification strategy. We have now developed an expression system for the production of small peptides by recombinant means at high yield, including when the peptide is a component of a larger fusion protein. Data will be presented on the recombinant production and purification of antifungal peptides from bacteria. In addition, we

linked antifungal peptides to a protein carrier to initiate peptide engineering studies with these recombinant fusion proteins. As with recombinant proteins, peptide fusions can be used to characterize and evolve the functional peptide unit.

L145 ANSWER 149 OF 199 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN The ice nucleation-active protein of Erwinia ananas IN-10 (inaA protein) AB was over-expressed as inclusion bodies in Escherichia coli YA21 harboring plasmid pINA6S13. The inaA protein was purified from inclusion bodies by repeated solubilization with Triton X-100 to obtain a protein preparation free from sugar and lipid. The yield was 15.3 mg of inaA protein from 60 mg of bacterial cells on a dry weight basis. The N-terminal amino acid sequence of the purified inaA protein was Met-Lys-Glu-Asp-Lys-Val-Leu-Ile-Leu, which agreed exactly with that predicted from the inaA gene. The amino acid composition corresponded approximately with that predicted from the sequence of the inaA gene. The small deviation from the predicted value may have been a result of the very high mol.weight, 130,000, of the inaA protein. purified protein showed ice nucleation activity, indicating that the inaA protein per se was able to act as an ice nucleus. The study establishes a simplified and enlarged system for the production of pure inaA protein. The protein could be used for the mild freeze-concentration of foods and other materials sensitive to deep-freezing. (20 ref)

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L170 ANSWER 1 OF 5
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    Differential gene expression for investigation of Escherichia coli biofilm
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     Applied and environmental microbiology, (2005 Jul) Vol. 71, No. 7, pp.
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     Ren Dacheng; Zuo Rongjun; Gonzalez Barrios Andres F; Bedzyk Laura A;
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     PCT Int. Appl., 37 pp.
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     Phadtare, Sangita; Kato, Ikunoshin; Inouye, Masayori
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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     Abstracts of the General Meeting of the American Society for Microbiology,
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Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).

Terry, L. J. [Reprint Author]; Gumulak-Smith, J. J. [Reprint Author]; ΑU Forsyth, M. H. [Reprint Author]

AN 2003:519056 BIOSIS

SO

MEDLINE on STN DUPLICATE 3 L170 ANSWER 4 OF 5

The luxS gene is involved in cell-cell signalling for toxin production in Clostridium perfringens.

Molecular microbiology, (2002 Apr) Vol. 44, No. 1, pp. 171-9. SO Journal code: 8712028. ISSN: 0950-382X.

Ohtani Kaori; Hayashi Hideo; Shimizu Tohru AU

2002230093 MEDLINE AN

L170 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN Characterization of quorum sensing pathways in E. coli.

Abstracts of the General Meeting of the American Society for Microbiology, SO (1999) Vol. 99, pp. 363. print. Meeting Info.: 99th General Meeting of the American Society for Microbiology. Chicago, Illinois, USA. May 30-June 3, 1999. American Society for Microbiology. ISSN: 1060-2011.

Rather, P. N. [Reprint author]; Baca-Delancey, R. R. [Reprint author]; ΑIJ Ding, X. [Reprint author]

1999:311307 BIOSIS AN

## => d ab 3-5

L170 ANSWER 3 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN Background: Helicobacter pylori is one of a diverse array of bacterial species with a density-dependent signal system. We previously demonstrated that H. pylori produces autoinducer-2 (AI-2) as a quorum sensing molecule and that luxS is involved in its prodution. LuxS is the third gene in a putative three-gene operon ( cysK, metB, luxS). cysK and metB encode enzymes critical to amino acid synthesis. The mechanism of synthesis and detection of AI-2 by H. pylori has not fully been elucidated, and the relationship between production of AI-2 and growth phase has received little attention. hypothesize that CysK, MetB, and LuxS are part of the same metabolic pathway. Additionally, this study aims to examine the kinetics of AI-2 production in H. pylori. Methods: In order to characterize the production of AI-2 in H. pylori during other phases of growth, we isolated conditioned media (CM) from cultures of H. pylori J99 and 26695 at several

points during growth. The CM generated was assayed for AI-2 levels utilizing a Vibrio harveyi bioassay. We have generated a 26695 derivative, L26-3, that is a luxS merodiploid, containing an ectopic copy of luxS in ureA. We have also generated a H. pylori strain 26695 derivative (L26-4) with the genotype cysk::CAT ure::luxS/ aphA3. 26695, L26-3 and L26-4 were grown in broth to mid-log phase, and CM was generated. This CM was assayed for AI-2 using a V. harveyi bioassay. Results: While previous results have demonstrated that H. pylori strain 60190 has maximal AI-2 production in mid-log phase and that AI-2 production is greatly reduced in stationary phase cultures, we find that H. pylori strains 26695 and J99 putatively continue to produce AI-2 through stationary phase. Preliminary analysis of L26-3 revealed increased levels of AI-2 production. Analysis of L26-4 CM suggests that cysK may not be essential for AI-2 synthesis. Conclusions: The variation in AI-2 production through the phases of culture growth suggests that the production of AI-2 varies by H. pylori strain. Further analysis of the pathway leading to AI-2 production may serve to clarify the significance of this molecule in regulating gene expression in H. pylori.

L170 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 3 A Gram-positive anaerobic pathogen, Clostridium perfringens, causes clostridial myonecrosis or gas gangrene in humans by producing numerous extracellular toxins and enzymes that act in concert to degrade host tissues. C. perfringens possesses a homologue of the luxS gene that is reported to be responsible for the production of autoinducer 2 (AI-2), which participates in quorum sensing in bacteria. The luxS mutant was constructed using C. perfringens strain 13, and the role of the luxS gene in toxin production was examined. The cell-free culture supernatant from wild-type strain 13 greatly stimulated the luminescence of Vibrio harveyi BB170, whereas that from the luxS mutant caused no significant stimulation, indicating that the luxS gene is necessary for AI-2 production in C. perfringens. The luxS mutant showed a reduced level of production of alpha-, kappa- and theta-toxins. In the luxS mutant, the transcription of the theta-toxin gene (pfoA) was lower at mid-exponential growth phase, whereas alpha- and kappa-toxin gene transcription was not significantly affected. The production of toxins in the luxS mutant was stimulated by the addition of the culture supernatant from the wild-type cells, possibly because of the presence of AI-2. Moreover, the expression of the pfoA gene in the luxS mutant was apparently activated when the mutant cells were cultured in the presence of culture supernatants from the wild-type C. perfringens, Escherichia coli DH5alpha carrying the luxS gene of C. perfringens. A deletion analysis of the luxS operon showed that the luxS gene alone is responsible for cell-cell signalling, and that the metB or cysK genes located upstream of luxS are not involved in regulating toxin production. Our results indicate that cell-cell signalling by AI-2 plays an important role in the regulation of toxin production in C. perfringens.

L170 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

FILE 'BIOSIS'

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L175 0 L150 AND L53
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FILE 'EMBASE'

L176 1 L151 AND L54

FILE 'HCAPLUS'

L177 0 L152 AND L55

FILE 'NTIS'

L178 0 L153 AND L56

FILE 'ESBIOBASE'

L179 0 L154 AND L57

FILE 'BIOTECHNO'

L180 0 L155 AND L58

FILE 'WPIDS'

L181 0 L156 AND L59

TOTAL FOR ALL FILES

L182 1 L157 AND L60

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L182 ANSWER 1 OF 1 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

TI Acyl-homoserine lactone acylase from Ralstonia strain XJ12B represents a novel and potent class of quorum-quenching enzymes.

SO Molecular Microbiology, (2003) Vol. 47, No. 3, pp. 849-860.

Refs: 58

ISSN: 0950-382X CODEN: MOMIEE

AU Lin Y.-H.; Xu J.-L.; Hu J.; Wang L.-H.; Leong Ong S.; Renton Leadbetter J.; Zhang L.-H.

AN 2003041693 EMBASE

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L182 ANSWER 1 OF 1 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

N-acylhomoserine lactones (AHLs) are used as signal molecules by many AB quorum-sensing Proteobacteria. Diverse plant and animal pathogens use AHLs to regulate infection and virulence functions. These signals are subject to biological inactivation by AHL-lactonases and AHL-acylases. Previously, little was known about the molecular details underlying the latter mechanism. An AHL signal-inactivating bacterium, identified as a Ralstonia sp., was isolated from a mixed-species biofilm. The signal inactivation encoding gene from this organism, which we callaiiD, was cloned and successfully expressed in Escherichia coli and inactivated three AHLs tested. The predicted 794-amino-acid polypeptide was most similar to the aculeacin A acylase (AAC) from Actinoplanes utahensis and also shared significant similarities with cephalosporin acylases and other N-terminal (Ntn) hydrolases. However, the most similar homologues of AiiD are deduced proteins of undemonstrated function from available Ralstonia, Deinococcus and Pseudomonas genomes. LC-MS analyses demonstrated that AiiD hydrolyses the AHL amide, releasing homoserine lactone and the corresponding fatty acid. Expression of AiiD in Pseudomonas aeruginosa PAO1 quenched quorum sensing by this bacterium, decreasing its ability to swarm, produce elastase and pyocyanin and to paralyse nematodes. Thus, AHL-acylases have fundamental implications and hold biotechnological promise in quenching quorum sensing.

=> s 1157 and 184

FILE 'MEDLINE'

L183 8 L146 AND L73

FILE 'SCISEARCH'

L184 10 L147 AND L74

FILE 'LIFESCI'

L185 9 L148 AND L75

FILE 'BIOTECHDS'

L186 7 L149 AND L76

FILE 'BIOSIS'

L187 8 L150 AND L77

FILE 'EMBASE'

L188 9 L151 AND L78

FILE 'HCAPLUS'

L189 10 L152 AND L79

FILE 'NTIS'

L190 0 L153 AND L80

FILE 'ESBIOBASE'

L191 12 L154 AND L81

FILE 'BIOTECHNO'

L192 8 L155 AND L82

FILE 'WPIDS'

L193 1 L156 AND L83

TOTAL FOR ALL FILES

L194 82 L157 AND L84

=> s 1194 not 2004-2006/py

FILE 'MEDLINE'

1332548 2004-2006/PY

(20040000-20069999/PY)

L195 6 L183 NOT 2004-2006/PY

FILE 'SCISEARCH'

2454856 2004-2006/PY

(20040000-20069999/PY)

L196 6 L184 NOT 2004-2006/PY

FILE 'LIFESCI'

189530 2004-2006/PY

L197 8 L185 NOT 2004-2006/PY

FILE 'BIOTECHDS'

56959 2004-2006/PY

L198 4 L186 NOT 2004-2006/PY

FILE 'BIOSIS'

1023506 2004-2006/PY

L199 6 L187 NOT 2004-2006/PY

FILE 'EMBASE'

1117159 2004-2006/PY

L200 7 L188 NOT 2004-2006/PY

FILE 'HCAPLUS'

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2548350 2004-2006/PY
L201
             6 L189 NOT 2004-2006/PY
FILE 'NTIS'
         25986 2004-2006/PY
L202
             0 L190 NOT 2004-2006/PY
FILE 'ESBIOBASE'
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             9 L191 NOT 2004-2006/PY
L203
FILE 'BIOTECHNO'
           586 2004-2006/PY
L204
             8 L192 NOT 2004-2006/PY
FILE 'WPIDS'
       2489972 2004-2006/PY
L205
             0 L193 NOT 2004-2006/PY
TOTAL FOR ALL FILES
            60 L194 NOT 2004-2006/PY
L206
=> dup rem 1206
PROCESSING COMPLETED FOR L206
L207
             14 DUP REM L206 (46 DUPLICATES REMOVED)
=> d tot
      ANSWER 1 OF 14 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
L207
ΤI
      Method of regulating genes in microorganisms, useful for e.g. increasing
      production of recombinant proteins, comprises
      treating gene-containing microorganism with 4,5-dihydroxy-2-cyclopenten-1-
      one;
         gene expression regulation and DNA array useful for
         recombinant protein promotion
      PHADTARE S; KATO I; INOUYE M
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AN
      2003-25814 BIOTECHDS
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                                COPYRIGHT 2006 CSA on STN DUPLICATE 1
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     Characterization of RAP, a quorum sensing activator of
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     Staphylococcus aureus
     FEMS Microbiology Letters [FEMS Microbiol. Lett.], (20030627) vol. 223,
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     no. 2, pp. 167-175.
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     Korem, M.; Sheoran, A.S.; Gov, Y.; Tzipori, S.; Borovok, I.; Balaban, N.*
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L207 ANSWER 3 OF 14 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
      Crystal of LuxS protein which is involved in production of autoinducer-2
TI
      for identifying modulators useful for treating e.g. infection disease,
      stomach cancer, stomach ulcer and other intestinal complications;
         vector-mediated gene transfer, expression in host cell and
         computer bioinformatic software for recombinant
         protein production and drug screening
      LEWIS H A
ΔΙΙ
      2002-18835 BIOTECHDS
\Delta M
      WO 2002038595 16 May 2002
PΙ
                                                         DUPLICATE 2
L207 ANSWER 4 OF 14
                        MEDLINE on STN
     Genes encoding the N-acyl homoserine lactone-degrading enzyme are
     widespread in many subspecies of Bacillus thuringiensis.
     Applied and environmental microbiology, (2002 Aug) Vol. 68, No. 8, pp.
SO
     3919-24.
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Journal code: 7605801. ISSN: 0099-2240.

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- L207 ANSWER 5 OF 14 LIFESCI COPYRIGHT 2006 CSA on STN DUPLICATE 3
- TI LuxS-dependent quorum sensing in Porphyromonas gingivalis modulates protease and haemagglutinin activities but is not essential for virulence
- SO Microbiology, (20020300) vol. 148, no. 3, pp. 763-772. ISSN: 1350-0872.
- AU Burgess, N.A.; Kirke, D.F.; Williams, P.; Winzer, K.; Hardie, K.R.; Meyers, N.L.; Aduse-Opoku, J.; Curtis, M.A.; Camara, M.
- AN 2002:77596 LIFESCI
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- SO Journal of biotechnology, (2002 Jan 18) Vol. 92, No. 3, pp. 237-49. Journal code: 8411927. ISSN: 0168-1656.
- AU Han Ling; Doverskog Magnus; Enfors Sven-Olof; Haggstrom Lena
- AN 2001639835 MEDLINE
- L207 ANSWER 7 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
- TI Bacterial autoinduction: Looking outside the cell for new metabolic engineering targets.
- SO Microbial Cell Factories, (20 Dec 2002) Vol. 1, pp. 9p. . Refs: 91 ISSN: 1475-2859 CODEN: MCFICT
  - DeLisa M.P.; Bentley W.E.
- AN 2004253557 EMBASE
- L207 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
- TI Bacterial autoinduction: looking outside the cell for new metabolic engineering targets
- SO Microbial Cell Factories (2002), 1, No pp. given
  CODEN: MCFICT; ISSN: 1475-2859
  URL: http://www.microbialcellfactories.com/content/pdf/1475-2859-1-5.pdf
- AU DeLisa, Matthew P.; Bentley, William E.
- AN 2004:815256 HCAPLUS
- DN 141:422094

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- TI Mapping stress-induced changes in autoinducer AI-2 production in chemostat-cultivated Escherichia coli K-12.
- SO Journal of bacteriology, (2001 May) Vol. 183, No. 9, pp. 2918-28. Journal code: 2985120R. ISSN: 0021-9193.
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- AN 2001270821 MEDLINE
- L207 ANSWER 10 OF 14 MEDLINE on STN DUPLICATE 6
- TI Quorum signaling via AI-2 communicates the "Metabolic Burden" associated with heterologous protein production in Escherichia coli.
- SO Biotechnology and bioengineering, (2001 Nov 20) Vol. 75, No. 4, pp. 439-50.

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- AU DeLisa M P; Valdes J J; Bentley W E
- AN 2001565037 MEDLINE
- L207 ANSWER 11 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
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13C NMR spectroscopy.

SO Journal of Biotechnology, (18 January, 2001) Vol. 92, No. 3, pp. 237-249. print.

CODEN: JBITD4. ISSN: 0168-1656.

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- AU Weikert C.; Canonaco F.; Sauer U.; Bailey J.E.
- CS U. Sauer, Institute of Biotechnology, ETH Zurich, CH-8093 Zurich, Switzerland.

E-mail: sauer@biotech.biol.ethz.ch

- SO Metabolic Engineering, (2000), 2/4 (293-299), 34 reference(s) CODEN: MEENFM ISSN: 1096-7176
- DT Journal; Article
- CY United States
- LA English
- SL English
- L207 ANSWER 13 OF 14 MEDLINE on STN DUPLICATE 7
- TI Characterization of the SarA virulence gene regulator of Staphylococcus aureus.
- SO Molecular microbiology, (1999 Jul) Vol. 33, No. 2, pp. 307-16. Journal code: 8712028. ISSN: 0950-382X.
- AU Rechtin T M; Gillaspy A F; Schumacher M A; Brennan R G; Smeltzer M S; Hurlburt B K
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- SO Molecular microbiology, (1998 Jul) Vol. 29, No. 1, pp. 219-34. Journal code: 8712028. ISSN: 0950-382X.
- AU Liu Y; Cui Y; Mukherjee A; Chatterjee A K
- AN 1998367138 MEDLINE

## => d ab tot

L207 ANSWER 1 OF 14 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN AB DERWENT ABSTRACT:

NOVELTY - Method for regulating a gene (I) in a microorganism comprises treating gene-containing microorganism with 4,5-dihydroxy-2-cyclopenten-1-one (DHCP). (I) encodes a ribosomal protein or a protein of known or unknown function or is involved in the response to stress, membrane synthesis or function, or general metabolism.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a method (M1) of screening for physiologically active compounds (A) by determining the expression level of genes that are modulated by DHCP; (2) (A) identified by (M1); (3) a method (M2) for increasing production of a recombinant polypeptide in a microorganism by culturing it in presence of DHCP; (4) a method (M3) for inhibiting an activity of an interspecies quorum-sensing inducer, using DHCP; and (5) a composition, containing DHCP, for: (a) regulating quorum

composition, containing DHCP, for: (a) regulating quorum sensing; (b) regulating expression of specific genes;

- (c) promoting secretion of recombinant proteins; or
- (d) maintaining homeostasis.

ACTIVITY - None given.

MECHANISM OF ACTION - Gene Expression Regulator. Escherichia coli

JM83 was incubated in presence of 250 microM 4,5-dihydroxy-2-cyclopenten1-one (DHCP), then RNA isolated and used to probe DNA arrays that
represent all open-reading frames of E. coli K-12 W3110. Expression
levels were compared with those in untreated cells. Most genes encoding
ribosomal L proteins were downregulated (treated:control ratio
0.23-0.49); also (1) 40 genes encoding cell membrane-related proteins
were affected, mostly downregulated but some, e.g. creD (unknown
function) and tehA (tellurite resistance) were upregulated; (2) the rpoS
gene, and genes regulated by the RpoS (a global stress-response
regulator) protein were upregulated; (3) 44 genes involved in general
metabolism were affected, particularly those implicated in Cys
biosynthesis were upregulated and (4) 54 other genes, some of unknown
function, were also modified, especially genes involved in resistance to
tellurite and oxidative stress were upregulated. DHCP also eliminates the
effect of the quorum-sensing inducer AI-2.

USE - The method uses DHCP as a regulator of a wide range of bacterial genes to: (1) manufacture a composition for regulating a gene in a microorganism; (2) inhibit activity of interspecies quorum -sensing inducers (quorum-sensing is associated with virulence, motility and outer membrane function); (3) promote secretion of recombinant proteins; and (4) maintain homeostasis (all claimed).(37 pages)

COPYRIGHT 2006 CSA on STN DUPLICATE 1 L207 ANSWER 2 OF 14 LIFESCI Staphylococcus aureus are Gram-positive bacteria and cause diverse serious diseases in humans and animals through the production of toxins. The production of toxins is regulated by quorum sensing mechanisms, where proteins such as RNAIII activating protein (RAP) are secreted by the bacteria and induce virulence. Antibodies to RAP have been shown to protect mice from infection, but the molecular structure of RAP was not known and hindered vaccine development. To characterize RAP, recombinant protein was made and tested for its ability to induce genes important for pathogenesis (agr). In addition, monoclonal antibodies were produced to identify its cellular localization. Results shown here indicate that RAP is a 277-aa protein that is an ortholog of the ribosomal protein L2. Like the native molecule, recombinant RAP activates the production of RNAIII (encoded by agr). Using RAP specific monoclonal antibodies we demonstrate that RAP is continuously secreted and while RAP is expressed also in other bacteria (like Staphylococcus epidermidis, Staphylococcus xylosus and Escherichia coli), it is secreted to the culture medium only by S. aureus. Our results show that the ribosomal protein L2 has an extraribosomal function and that when secreted RAP acts as an autoinducer of virulence to regulate S. aureus pathogenesis.

L207 ANSWER 3 OF 14 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN AB DERWENT ABSTRACT:

NOVELTY - A crystal (I) comprising LuxS protein (which is involved in the production of autoinducer-2 (AI-2), an intercellular signaling molecule employed in the **quorum sensing** pathway of various bacteria) or a functional LuxS protein subunit in crystalline form, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a crystal (II) comprising a homolog of LuxS protein having a root mean square deviation of the alpha-carbon atoms of less than 2.0 Angstrom; (2) making (M1) (II) by mixing a volume of a solution comprising the LuxS protein with a volume of a reservoir solution comprising a precipitant and incubating the mixture obtained over the reservoir solution in a closed container, under conditions suitable for crystallization until the crystal forms; (3) determining (M2) the three-dimensional structure of a LuxS protein crystal, by providing (I) or (II) and analyzing the crystal by X-ray diffraction; (4) a machine-readable medium embedded with: (a) information that corresponds to a three-dimensional structural representation of (I) or (II); (b) molecular structure coordinates as shown in the specification or at least

50% of the coordinates; or (c) molecular structure coordinates of a protein molecule comprising LuxS protein binding pocket comprising at least three amino acids from Glu60, Arg68, Ile81 and Asp80, Ala64, His61, Tyr91, Ser9, Phe10 and Leu7, His14, Arg23, Asp40, Arg42, Met84, Cys86 and Thr88 having the structure coordinate as shown in the specification or by the structure coordinates of a binding pocket homolog where the root mean square deviation of the backbone atoms of the amino acid residues of the binding pocket and the binding pocket homolog is less than 2.0 Angstrom; (5) producing (M3) a mutant of LuxS protein having altered property related to LuxS protein by constructing a three-dimensional structure of LuxS protein having structure coordinates of (I)/(II); using modeling methods to identify in the three-dimensional structure at least one structural portion of the LuxS protein molecule, where an alteration in the structural portion is predicted to result in the altered property; providing a nucleic acid molecule having a modified sequence that encodes a deletion, insertion, or substitution of one or more amino acids at a position corresponding to the structural portion; and expressing the nucleic acid molecule to produce the mutant; (6) identifying (M4) a candidate binding compound capable of binding to the active site (or accessory binding site) of LuxS protein, by introducing into a computer program information derived from structural coordinates defining an active site (or accessory binding site) conformation of a LuxS protein molecule based upon three-dimensional structure determination comprising an active site (or accessory binding site) formed by at least the interaction of amino acids Glu, Arg, Ile and Asp where the program utilizes or displays their three-dimensional structure; generating a three-dimensional representation of the active site (or accessory binding site) cavity of the LuxS protein in the computer program; superimposing a model of the binding test compound on the model of the active site (or accessory binding site) of the LuxS protein; and assessing whether the test compound model fits spatially into the active site (or accessory binding site) of the LuxS protein; (7) selecting (M5) at least one compound that potentially binds to LuxS protein, by: (a) constructing a three-dimensional structure of LuxS protein and selecting at least one compound which potentially binds LuxS protein; (b) constructing a three-dimensional structure of a protein molecule comprising a LuxS protein binding pocket and computationally screening several compounds using the structure constructed; and (c) computationally screening a three-dimensional structural representation of a molecule comprising a LuxS protein binding pocket an identifying those that bind; (8) designing (M6) a compound that modulates LuxS protein activity by providing a computer modeling program with a set of structure coordinates, or a three-dimensional conformation derived from them, for a molecule that comprises a binding pocket having the structural coordinates of the binding pocket of LuxS protein, or a binding pocket homolog; computationally building a chemical entity represented by set of structure coordinates and determining whether the chemical entity is a modulator expected to bind to or interfere with the molecule; (9) a compound (C1) identified, designed or made by M4, M5 and M6; (10) a pharmaceutical composition comprising C1 or its salt and a carrier; (11) obtaining structural information about a molecule or a molecular complex of unknown structure by crystallizing the molecule or molecular complex; generating an x-ray diffraction pattern from the crystallized molecule or molecular complex and using a molecular replacement method to interpret the structure of the molecule, where the molecular replacement method uses the structure coordinates as given in the specification, or its subset, or the structure coordinates of the binding pocket; and (12) homology modeling a LuxS protein homolog by: (a) aligning the amino acid sequence of LuxS protein homolog with an amino acid sequence of LuxS protein; (b) incorporating the sequence of homolog into a model of the structure of LuxS protein; (c) subjecting the preliminary model to energy minimization to yield an energy minimized model; and (d) remodeling regions of the energy minimized model where stereochemistry restraint are violated to yield a final model of the homolog.

BIOTECHNOLOGY - Preferred Crystal: (I) is preferably diffraction

quality, is an apo-crystal, a native crystal, and/or is a heavy-atom derivative crystal, where LuxS is Helicobacter pylori, Haemophilus influenze or Deinococcus radiodurans LuxS, or a mutant which is selenomethionine, selenocysteine mutant, conservative mutant, truncated or extended mutant. (I) is characterized by a set of structure coordinate that is substantially similar to the set of structure coordinates as given in the specification. (II) is produced by mixing a volume of a solution comprising the LuxS protein with a volume of a reservoir solution comprising a precipitant and incubating the mixture obtained over the reservoir solution in a closed container, under conditions suitable for crystallization until the crystal forms. Protein co-ordinate data is given in the patent specification. Preferred Method: In M3, the altered activity of LuxS protein is preferably altered binding activity or immunogenicity, where an epitope is altered. In M4, the structural coordinates correspond to the liganded or unliganded LuxS protein, and the binding compound is a LuxS inhibitor. M5 further comprises screening a library of compounds. The binding pocket comprises at least three amino acids from Glu60, Arg68, Ile81 and Asp80, Ala64, His61, Tyr91, Ser9, Phe10 and Leu7, His14, Arg23, Asp40, Arg42, Met84, Cys86 and Thr88 having the structure coordinate as shown in the specification or a molecule comprising a binding pocket homolog where the root mean square deviation of the backbone atoms of the amino acid residues of the binding pocket and the binding pocket homolog is less than 2.0 Angstrom. The method comprises determining whether the compound potentially binds to the molecule by performing a fitting operation between the compound and a binding pocket of the molecule or molecular complex, and computationally analyzing the results of the fitting operation to quantify the association between, or the interference with, the compound and the binding pocket.

ACTIVITY - Antibacterial; Cytostatic; Antiulcer. No supporting biological data is given.

MECHANISM OF ACTION - LuxS protein modulator (claimed). No supporting biological data is given.

USE - C1 is useful for modulating LuxS protein activity (claimed), useful for treating e.g. infection disease, stomach cancer, stomach ulcer and other intestinal complications.

ADMINISTRATION - C1 is administered through oral, buccal, sublingual, rectal, transdermal, vaginal, transmucosal, nasal or intestinal administration, parenteral delivery, including intramuscular, subcutaneous, intramedullar injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal or intraocular injections. Dosage of C1 is for 0.01-1000 (preferably 10-30) mg/day.

EXAMPLE - An open-reading frame for LuxS was amplified from Helicobacter pylori (Hp-ATCC43504D) genomic DNA by the polymerase chain reaction (PCR) using the following primers: Forward primer GGATTTCACATATGAAAATGAATGTAGAGAGTTTC, Reverse Primer: GTTCGGATCCAACCCCACTTCAGACC. The PCR product (456 bp expected) was digested with NdeI and BamHI, electrophoresed on a 1% agarose gel in TBE buffer and the appropriate size band was excised from the gel and eluted using a standard gel extraction kit. The eluted DNA was ligated overnight with T4 DNA ligase at 16 degreesC into pSB3, previously digested with NdeI and BamHI. The vector pSB3 was a modified version of pET26b where the following sequence had been inserted into the BamHI siteL GGATCCCACCACCACCACCACCACTGAGATCC. The resulting sequence of the gene after being ligated into the vector, from the Shine-Dalgarno sequence through the stop site and the original BamHI, site was as follows: AAGGAGGAGATATACATATG(open reading frame (ORF))GGATCCCACCACCACCACCACCACTGA GATCC. The LuxS expressed using this vector had 8 amino acids to the C-terminal end (Gly-Ser-His-His-His-His-His-His). Plasmids containing ligated inserts were transformed into chemically competent Escherichia coli such as Top 10 cells. Colonies were then screened for inserts in the correct orientation and miniprepped. The miniprep DNA was transformed into BL21 (DE3) Active Motif cells and plated onto petri dishes containing Luria-Bertani medium (LB) agar with 30 mug/ml of kanamycin. Isolated, single colonies were grown to mid-log phase and stored at -80

degrees Centigrade in LB containing 15% glycerol. LuxS containing selenomethionine was overexpressed in Escherichia coli and the cultures were allowed to ferment overnight and the LuxS was purified. For crystals of Helicobacter pylori from which the molecular structure coordinates of were obtained, it had been found that a hanging drop containing 1 microlitre of LuxS polypeptide 5 mg/mL in 10 mM HEPES pH 7.5, 150 mM NaCl, 1 mM betaME, 10 mM methionine, and 1 microlitre reservoir solution 32% (w/v) PEG1000, 200 mM ammonium sulfate, 2 mM beta-mercaptoethanol, and 100 mM MES, pH 5.75 in a sealed container containing 500 microlitres reservoir solution, incubated for 3-7 days at 20 degrees Centigrade provide diffraction quality crystals.(473 pages)

L207 ANSWER 4 OF 14 MEDLINE on STN DUPLICATE 2 Gram-negative bacteria can communicate with each other by N-acyl homoserine lactones (AHLs), which are quorum-sensing autoinducers. Recently, the aiiA gene (encoding an enzyme catalyzing the degradation of AHL) has been cloned from Bacillus sp. strain 240B1. During investigations in the course of the ongoing Bacillus thuringiensis subsp. morrisoni qenome project, an aiiA homologue gene in the genome sequence was found. These results led to consideration of the possibility of the widespread existence of the gene in B. thuringiensis. aiiA homologue genes were found in 16 subspecies of B. thuringiensis, and their sequences were determined. Comparison of the Bacillus sp. strain 240B1 aiiA gene with the B. thuringiensis aiiA homologue genes showed high homologies of 89 to 95% and 90 to 96% in the nucleotide sequence and deduced amino acid sequence, respectively. Among the subspecies of B. thuringiensis having an aiiA gene, the subspecies aizawai, galleriae, kurstaki, kyushuensis, ostriniae, and subtoxicus were shown to degrade AHL. It was observed that recombinant Escherichia coli producing AiiA proteins also had AHL-degrading activity and could also attenuate the plant pathogenicity of Erwinia carotovora. These results indicate that insecticidal B. thuringiensis strains might have potential to compete with gram-negative bacteria in natural ecosystems by autoinducer-degrading activity.

L207 ANSWER 5 OF 14 LIFESCI COPYRIGHT 2006 CSA on STN DUPLICATE 3 Porphyromonas gingivalis is a Gram-negative black-pigmented obligate anaerobe implicated in the aetiology of human periodontal disease. The virulence of P. gingivalis is associated with the elaboration of the cysteine proteases Arg-gingipain (Rgp) and Lys-gingipain (Kgp), which are produced at high bacterial cell densities. To determine whether quorum sensing plays a role in the regulation of Rgp and Kgp, biosensors capable of detecting either N-acylhomoserine lactone (AHLs) or the luxS-dependent autoinducer (AI-2) quorumsensing signalling molecules in spent culture supernatants were first employed. While no AHLs could be detected, the Vibrio harveyi BB170 biosensor was activated by spent P. gingivalis W50 culture supernatants. The P. gingivalis luxS gene was cloned and demonstrated to restore AI-2 production in the Escherichia coli luxS mutant DH5 alpha . Mutation of luxS abolished AI-2 production in P. gingivalis. Western blotting using antibodies raised against the recombinant protein revealed that LuxS levels increased throughout growth even though AI-2 activity was only maximally detected at the mid-exponential phase of growth and disappeared by the onset of stationary phase. Similar results were obtained with E. coli DH5 alpha transformed with luxS, suggesting that AI-2 production is not limited by a lack of LuxS protein. Analysis of Rgp and Kgp protease activities revealed that the P. gingivalis luxS mutant produced around 45% less Rgp and 30% less Kgp activity than the parent strain. In addition, the luxS mutant exhibited a fourfold reduction in haemagglutinin titre. However, these reductions in virulence determinant levels were insufficient to attenuate the luxS mutant in a murine lesion model of P. gingivalis infection.

L207 ANSWER 6 OF 14 MEDLINE on STN DUPLICATE 4
AB Addition of selected amino acids could be a means to improve

production of recombinant proteins in industrial processes. We found that glycine increased the maximum specific growth rate of Escherichia coli from 0.67 to 0.78 h(-1), and the cell yield from 0.57 to 0.98 g dry weight per g substrate, when supplemented to batch cultures in a glucose-mineral medium. Maximum effect occurred at pH 6.8, at a glycine concentration of 6-12 mmol l(-1), and at cell densities below 1.15 g dry weight 1(-1) (0D(610).3). When glycine was added to a culture at a cell density of 1.15 g l(-1) or above, no growth promoting effect of glycine was seen. The 'glycine effect' was not due to CO(2) produced by the glycine cleavage system (GCV), and the lack of effect at higher cell densities was not masked by acetate accumulation, but coincided with increased acetate production. The metabolism of glycine was further investigated in cultures supplied with [2-(13)C] labelled glycine, and the redistribution of label in the [1-(13)C], [2-(13)C], and [1,2-(13)C] isotopomeres of excreted acetate was analysed by 13C NMR. The NMR data revealed that very little degradation of glycine occurred at cell densities below 1.15 g l(-1). Simultaneously the biosynthesis of serine and glycine was repressed as judged by the absence of [2-(13)C] acetate, implying that added glycine was used as a source of glycine, serine, one-carbon units, and threonine. At cell densities above 1.15 g l(-1), 53% of the consumed glycine carbon was excreted as acetate. Degradation of glycine was associated with an increased uptake rate, cleavage by GCV, and degradation of both glycine-derived serine, and glucose-derived serine to pyruvate. switch in metabolism appears to be regulated by quorum sensing.

- L207 ANSWER 7 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
- AB Recent evidence has demonstrated that cell-to-cell signaling is a fundamental activity carried out by numerous microorganisms. A number of specialized processes are reported to be regulated by density-dependent signaling molecules including antibiotic production, bioluminescence, biofilm formation, genetic competence, sporulation, swarming motility and virulence. However, a more centralized role for quorum sensing is emerging where quorum signaling pathways overlap with stress and starvation circuits to regulate cellular adaptation to changing environmental conditions. The interplay of these phenomena is especially critical in the expression of recombinant proteins where elicitation of stress responses can dramatically impact cellular productivity. .COPYRGT. 2002 DeLisa and Bentley; licensee BioMed Central Ltd.
- L207 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2006 ACS on STN
- AB A review. Recent evidence has demonstrated that cell-to-cell signaling is a fundamental activity carried out by numerous microorganisms. A number of specialized processes are reported to be regulated by d.-dependent signaling mols. including antibiotic production, bioluminescence, biofilm formation, genetic competence, sporulation, swarming motility and virulence. However, a more centralized role for quorum sensing is emerging where quorum signaling pathways overlap with stress and starvation circuits to regulate cellular adaptation to changing environmental conditions. The interplay of these phenomena is especially critical
  - in the expression of recombinant proteins where elicitation of stress responses can dramatically impact cellular productivity.
- L207 ANSWER 9 OF 14 MEDLINE on STN DUPLICATE 5

  AB Numerous gram-negative bacteria employ a cell-to-cell signaling mechanism, termed quorum sensing, for controlling gene expression in response to population density. Recently, this phenomenon has been discovered in Escherichia coli, and while pathogenic E. coli utilize quorum sensing to regulate pathogenesis (i.e., expression of virulence genes), the role of quorum

sensing in nonpathogenic E. coli is less clear, and in particular, there is no information regarding the role of quorum sensing during the overexpression of recombinant proteins. production of autoinducer AI-2, a signaling molecule employed by E. coli for intercellular communication, was studied in E. coli W3110 chemostat cultures using a Vibrio harveyi AI-2 reporter assay (M. G. Surrette and B. L. Bassler, Proc. Natl. Acad. Sci. USA 95:7046-7050, 1998). Chemostat cultures enabled a study of AI-2 regulation through steady-state and transient responses to a variety of environmental stimuli. Results demonstrated that AI-2 levels increased with the steady-state culture growth rate. In addition, AI-2 increased following pulsed addition of glucose, Fe(III), NaCl, and dithiothreitol and decreased following aerobiosis, amino acid starvation, and isopropyl-beta-Dthiogalactopyranoside-induced expression of human interleukin-2 (hIL-2). In general, the AI-2 responses to several perturbations were indicative of a shift in metabolic activity or state of the cells induced by the individual stress. Because of our interest in the expression of heterologous proteins in E. coli, the transcription of four quorum-regulated genes and 20 stress genes was mapped during the transient response to induced expression of hIL-2. Significant regulatory overlap was revealed among several stress and starvation genes and known quorum-sensing genes.

- MEDLINE on STN DUPLICATE 6 L207 ANSWER 10 OF 14 Recent reports have shown that bacterial cell-cell communication or quorum sensing is quite prevalent in pathogenic Escherichia coli, especially at high cell density; however, the role of quorum sensing in nonpathogenic E. coli is less clear and, in particular, there is no information regarding the role of quorum sensing in overexpression of plasmid-encoded genes. In this work, it was found that the activity of a quorum signaling molecule, autoinducer-2 (AI-2), decreased significantly following induction of several plasmid-encoded genes in both low and high-cell-density cultures of E. coli. Furthermore, we show that AI-2 signaling level was linearly related to the accumulation level of each protein product and that, in general, the highest rates of recombinant protein accumulation resulted in the greatest attenuation of AI-2 signaling. Importantly, our findings demonstrate for the first time that recombinant E. coli communicate the stress or burden of overexpressing heterologous genes through the quorum-based AI-2 signaling pathway. Copyright 2001 John Wiley & Sons, Inc.
- L207 ANSWER 11 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
- Addition of selected amino acids could be a means to improve AΒ production of recombinant proteins in industrial processes. We found that glycine increased the maximum specific growth rate of Escherichia coli from 0.67 to 0.78 h-1, and the cell yield from 0.57 to 0.98 g dry weight per g substrate, when supplemented to batch cultures in a glucose-mineral medium. Maximum effect occurred at pH 6.8, at a glycine concentration of 6-12 mmol 1-1, and at cell densities below 1.15 g dry weight 1-1 (0D610cntdot3). When glycine was added to a culture at a cell density of 1.15 g 1-1 or above, no growth promoting effect of glycine was seen. The 'glycine effect' was not due to CO2 produced by the glycine cleavage system (GCV), and the lack of effect at higher cell densities was not masked by acetate accumulation, but coincided with increased acetate production. The metabolism of glycine was further investigated in cultures supplied with (2-13C) labelled glycine, and the redistribution of label in the (1-13C), (2-13C), and (1,2-13C) isotopomeres of excreted acetate was analysed by 13C NMR. The NMR data revealed that very little degradation of glycine occurred at cell densities below 1.15 g 1-1. Simultaneously the biosynthesis of serine and glycine was repressed as judged by the absence of (2-13C) acetate, implying that added glycine was used as a source of glycine,

serine, one-carbon units, and threonine. At cell densities above 1.15 g 1-1, 53% of the consumed glycine carbon was excreted as acetate. Degradation of glycine was associated with an increased uptake rate, cleavage by GCV, and degradation of both glycine-derived serine, and glucose-derived serine to pyruvate. This switch in metabolism appears to be regulated by quorum sensing.

- L207 ANSWER 12 OF 14 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
- The Escherichia coli mutant CWML2 was previously reported to exhibit AB improved physiological characteristics, including recombinant protein production. Here we investigate the molecular basis of this phenotype by comparing the cellular level of three RNA polymerase sigma subunits by immunoblot analysis. While the level of housekeeping o.sup.D was similar in parent and mutant, the levels of the flagella synthesis regulator o.sup.F and the stationary phase regulator o.sup.S were higher in the mutant strain, indicating a different motility and stationary phase phenotype. Evidence for this conclusion was provided by the significantly higher motility of CWML2, compared to its parent. Based on these results, we hypothesized that alterations in ppGpp regulation via a homoserine lactone-dependent mechanism may be relevant for the mutant phenotype. Indeed, transcription of the rspAB operon, which was previously described to be involved in the degradation of homoserine lactone, was found to be deregulated in CWML2 in a plasmid-based reporter protein assay. By overexpression of the E. coli rspAB operon, we could partly mimic the mutant phenotype and demonstrate that co-overexpression of RspAB is a pertinent metabolic engineering strategy to improve recombinant protein production. . COPYRGT. 2000 Academic Press.
- L207 ANSWER 13 OF 14 MEDLINE on STN Staphylococcus aureus is a potent human pathogen that expresses a large number of virulence factors in a temporally regulated fashion. Two pleiotropically acting regulatory loci were identified in previous mutational studies. The agr locus comprises two operons that express a quorum-sensing system from the P2 promoter and a regulatory RNA molecule from the P3 promoter. The sar locus encodes a DNA-binding protein that activates the expression of both agr operons. have cloned the sarA gene, expressed SarA in Escherichia coli and purified the recombinant protein to apparent homogeneity. The purified protein was found to be dimeric in the presence and absence of DNA and to consist mostly of alpha-helices. DNase I footprinting of SarA on the putative regulatory region cis to the agr promoters revealed three high-affinity binding sites composed of two half-sites each. Quantitative electrophoretic mobility shift assays (EMSAs) were used to derive equilibrium binding constants (KD) for the interaction of SarA with these binding sites. An unusual ladder banding pattern was observed in EMSA with a large DNA fragment including all three

binding sites. Our data indicate that SarA regulation of the agr operons

involves binding to multiple half-sites and may involve other sites

located downstream of the promoters.

DUPLICATE 7

DUPLICATE 8 L207 ANSWER 14 OF 14 MEDLINE on STN The enterobacterium Erwinia carotovora ssp. carotovora strain 71 (hereafter Ecc71) produces extracellular enzymes such as pectate lyase isozymes (Pels), cellulase (Cel), polygalacturonase (Peh) and protease (Prt). These enzymes degrade plant cell wall components and are largely responsible for the elicitation of soft-rot diseases in plants and plant products. Ecc71 also produces HarpinEcc, the elicitor of hypersensitive reaction (HR) and the quorum-sensing signal, N-(3-oxohexanoyl)-L-homoserine lactone (OHL). OHL controls extracellular enzyme and HarpinEcc production. The levels of these enzymes, as well as the expression of hrpNEcc, the structural gene for HarpinEcc, and ohll, the gene specifying OHL synthesis, are negatively regulated by RsmaA. rsmB, formerly aepH, on the other hand, positively regulates extracellular

enzyme production. 6His-RsmA recombinant protein purified from E. coli binds rsmB RNA as indicated by gel mobility shift assays. rsmB comprises 547 bp DNA, which is transcribed from a single start site immediately after a sigma70-like promoter. In Ecc71, two rsmB RNA species are detected: a full-length 479 base rsmB RNA and a 259 base rsmB' RNA. rsmB' DNA hybridizes with the 259 base and the 479 base transcripts. A 3' RNase protection assay revealed that the 259 base and the 479 base RNA species end at the same position immediately after the putative rho-independent terminator. The expression of rsmB-lacZ transcriptional fusions established that the rsmB' RNA is not produced because of the activation of an internal promoter. These data strongly suggest that the 259 base rsmB' RNA is derived by processing of the primary rsmB RNA. In Ecc71, rsmB' expression driven by the lac promoter causes overproduction of Pel, Peh, Cel and Prt, and accumulation of pel-1, peh-1, hrpNEcc and ohll transcripts. By contrast, a plasmid with the rsmB' DNA sequence deleted fails to cause overproduction of the extracellular enzymes in Ecc71. The rsmB' effect also occurs in Escherichia coli as glycogen accumulation is stimulated in the presence of rsmB'. In vivo and in vitro translation as well as mutational analysis of rsmB' have established that rsmB' RNA does not yield a translational product. Therefore, we concluded that the rsmB' RNA itself functions as the regulator. Indeed, the expression rsmB' DNA leads to neutralization of the negative effects of the RNA-binding protein, RsmA, in Ecc71 and Serratia marcescens strain SM274. We propose a model that explains how RsmA and rsmB control the expression of genes for extracellular enzymes.

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